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Set	Items	Description
S1	185	CPG (S) ANTIGEN? (S) (DAY? OR HOUR?)
S2	74	RD (unique items)
S3	50	S2 (S) (MICE OR MOUSE)
S4	36	S2 (S) (ADMINIST? OR INNOCULAT?)

>>>KWIC option is not available in file(s): 399

4/3,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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14101812 BIOSIS NO.: 200300095841
A protective role of locally administered immunostimulatory CpG oligodeoxynucleotide in a mouse model of genital herpes infection.
AUTHOR: Harandi Ali M(a); Eriksson Kristina; Holmgren Jan
AUTHOR ADDRESS: (a)Department of Medical Microbiology and Immunology, Goteborg University Vaccine Research Institute (GUVAX), Guldhedsgatan 10A, 413 46, Goteborg, Sweden**Sweden E-Mail: ali.harandi@microbio.gu.se
JOURNAL: Journal of Virology 77 (2):p953-962 January 2003 2003
MEDIUM: print
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Unmethylated *CpG* dinucleotides in bacterial DNA or synthetic oligodeoxynucleotides (ODNs) are known as potent activators of the immune system and inducers of several Th1-associated immunomodulatory cytokines. We therefore investigated whether such a *CpG*-containing ODN (*CpG* ODN) given mucosally in the female genital tract could enhance innate immunity and protect against genital herpes infection. Groups of C57BL/6 mice were treated intravaginally with either *CpG* ODN or a non-*CpG* ODN control in the absence of any *antigen* either 2 *days* before or 4 h after an intravaginal challenge with a normally lethal dose of herpes simplex virus type 2 (HSV-2). Mice treated with *CpG* ODN exhibited significantly decreased titers of HSV-2 in their vaginal fluids compared with non-*CpG* ODN-treated mice. Furthermore, *CpG* ODN pretreatment significantly protected against development of disease and death compared to non-*CpG* ODN pretreatment. Most strikingly, *CpG* ODN conferred protection against disease and death even when given after the viral challenge. The *CpG* ODN-induced protection was associated with a rapid production of gamma interferon (IFN-gamma), interleukin-12 (IL-12), IL-18, and RANTES in the genital tract mucosa following *CpG* ODN treatment. The observed protection appeared to be dependent on IFN-gamma, IL-12, IL-18, and T cells, as *CpG* ODN pretreatment did not confer any significant protection in mice deficient in IFN-gamma, IL-12, IL-18, or T cells. Further, a complete protective immunity to reinfection was elicited in *CpG* ODN-treated, HSV-2-challenged mice, suggesting a role for mucosally *administered* *CpG* ODN in inducing the development of an acquired immune response in addition to its potent stimulation of innate immunity.

4/3,K/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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13715160 BIOSIS NO.: 200200343981
CD8+ response induced by CpG-peptide may probably require CD4 help for maintenance.
AUTHOR: Gierynska Malgorzata(a); Kumaraguru Uday; Lee Sujin; Rouse Barry T

AUTHOR ADDRESS: (a)Microbiology, University of Tennessee, 1414 Cumberland Avenue, Knoxville, TN, 37996**USA
JOURNAL: FASEB Journal 16 (4):pA680 March 20, 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: *CpG* oligodeoxynucleotides (*CpG* ODN) have proven to be excellent Th1 polarizing adjuvants. *Administered* with peptide or protein they generate population of *antigen* specific CTLs. C57BL/6 mice primed on *day* 0 and boosted on *day* 7 with SSIEFARL (HSV-1 gB498-505) mixed with bioactive *CpG* 1826 developed peptide specific CD8 response 7 *days* later, while mice immunized with control *CpG* 1982 did not. These CTLs produced IFNgamma upon peptide stimulation they were also capable of lysing specific targets. However, 60 *days* later, there was a quantitative difference between acute and memory response. The number of CD8/IFNgamma producing cells decreased during the time from 6% to 1.1%, and also their killing ability diminished from 43% to 19%. These data suggest that the maintenance of *antigen* specific population during the time may be is dependent on helper cell.

4/3,K/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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13715159 BIOSIS NO.: 200200343980
Mucosal immune responses induced by immunostimulatory oligonucleotides are enhanced when formulated in lipid particles.
AUTHOR: Yuan Zuan-Ning(a); Klimuk Sandra K(a); Semple Sean C(a)
AUTHOR ADDRESS: (a)Inex Pharmaceuticals Corp., 100-8900 Glenlyon Parkway, Burnaby, BC, V5J 5J8**Canada
JOURNAL: FASEB Journal 16 (4):pA680 March 20, 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Synthetic oligonucleotides containing immunostimulatory *CpG* motifs (ISS ODN) have been shown previously to be effective adjuvants for the induction of mucosal immune responses in experimental models. Recent studies have also...

...enhanced when entrapped in or associated with lipid particles. The aim of this study was to evaluate the induction of mucosal immune responses to specific *antigen* when various synthetic ODN were entrapped in lipid particles. Ovalbumin (OVA) was co-*administered* intranasally on *day* 0, 7 and 14 in a mixture that included ISS ODN or ISS ODN encapsulated in lipid particles. Three doses (1, 10, and 100 mg) of each ISS ODN were evaluated. Cholera toxin (CT) and non-*CpG* oligonucleotides were used as controls. On *day* 28, serum, lung washes and vaginal washes were collected and analyzed by ELISA. ISS ODN formulated in lipid particles significantly enhanced mucosal immune responses in...

4/3,K/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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13622857 BIOSIS NO.: 200200251678
Immunization with chaperonin 10 of Mycobacterium avium and CpG oligodeoxynucleotides inhibits M. avium multiplication in BALB/c mice.

AUTHOR: Fattorini L(a); Nisini R(a); Creti R(a); Fan Y(a); Serlupi-Crescenzi O(a); Stringaro A(a); Arancia G(a); Iona E(a); Orefici G(a)
AUTHOR ADDRESS: (a)Istituto Superiore di Sanita, Roma**Italy
JOURNAL: Abstracts of the General Meeting of the American Society for Microbiology 101p710-711 2001
MEDIUM: print
CONFERENCE/MEETING: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001
ISSN: 1060-2011
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: Chaperonin 10 (Cpn10) is produced in large amounts by mycobacteria and appears to be an immunodominant *antigen*. In this study recombinant M. avium Cpn10 was intranasally *administered* with a synthetic oligodeoxynucleotides containing unmethylated *CpG* motifs to examine protective efficacy against M. avium infection in mice. Methods: The Cpn10 gene of M. avium strain 485 (EMBL GenBank no. AF079544) was...

...coli M15 and purified by a Ni-NTA agarose affinity chromatography. Male BALB/c mice (6 mice/group) were immunized intranasally (20 mul/nostril) on *day* 0, 14, 28 with 10 mug Cpn10 or 10 mug *CpG* or 10 mug Cpn10+10 mug *CpG* or PBS. On *day* 42, mice were challenged intranasally with 103 or 2X104 M. avium (transparent colonial variant) CFU to mimic conditions of infection in humans. On *day* 42 after challenge, CFU numbers in lung and spleen were determined both in immunized and control mice. Results: When mice were challenged with 2X104 CFU, M. avium efficiently multiplied in lung and spleen (5.84+-0.27 and 3.21+-0.21 log10 CFU, respectively) as determined on *day* 42 in the control mice. Mice immunized with Cpn10+ *CpG* showed a significant CFU decrease (9.74 Log10 CFU, P=0.005) in the spleen when compared to controls, at odds with mice immunized with Cpn10 or *CpG* alone. The lung was not significantly protected at this challenge dose, then a lower dose (103 CFU) was tested. Under these conditions, on *day* 42 the log10 CFU numbers in lung and spleen of the control group were 4.8+-0.27 and 1.28+-1, respectively. While Cpn10 or *CpG* alone were not protective, a significant CFU decrease (0.43 Log10 CFU, P=0.045) in lung and CFU numbers lower than the detection limit of the method (3 CFU) in spleen were observed. Conclusions: While neither Cpn10 nor *CpG* alone restricted the growth of M. avium, the combination of the two provided a significant protection of lung and spleen against challenge doses similar to those found in the environment. These observations indicate that intranasal *administration* of *CpG* -containing adjuvants can be useful to increase the protective efficacy of M. avium Cpn10.

4/3,K/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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13591728 BIOSIS NO.: 200200220549
Endothelial cell-derived growth factor expands murine hematopoietic progenitor cells and DC precursor cells in vivo and increases the protective response to autologous tumor vaccination.
AUTHOR: McCormick Alison A(a); Davis Thomas(a); Wannberg Sharon(a); Tuse Daniel(a)
AUTHOR ADDRESS: (a)Large Scale Biology, Corp., Vacaville, CA**USA
JOURNAL: Blood 98 (11 Part 1):p701a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Dendritic cells (DC) are potent *antigen* processing and

presenting cells considered to be essential for initiating rapid and efficient immune responses, and possess the unique ability to stimulate naive T-cells and B-cells. Increasing vaccine potency by stimulating *antigen* uptake and presentation by DC has become a major area of research in the past 10 years. We have found that treating mice with porcine...

...EDHGF on vaccine potency, we pre-treated 6-8 week old, aged-matched female C3H/HEN mice (n=10) with EDHGF alone (one dose per *day*, subcutaneosly (s.c, 200 mug) for 7 consecutive *days*. Then, vaccine groups received 15 mug of protein derived from the 38C13 mouse B-cell lymphoma (a tumor-associated syngeneic self-*antigen* protein), s.c. at 2-week intervals for a total of two vaccinations. To ensure activation of DC at the site of vaccine injection, we mixed the vaccine with either control vehicle or 10 mug of *cpG* DNA oligomer (Hartman, et al., PNAS 1999, 96(16): 9305-10). Ten *days* after each vaccination, humoral anti-idiotypic immmunoglobulin levels were determined by ELISA. A pronounced anti-38C13 immune response was detected as early as 10 *days* following the first vaccination compared to control groups which had little or no detectable response. Isotype analysis revealed a predominantly IgG2a response after a single vaccination, suggesting early and robust Th1-type B-cell help. After two vaccinations, mice treated with EDHGF+vaccine, or vaccine alone in the absence of *cpG* immunization, had significantly lower serum anti-38C13 titers with little IgG2a isotype. Two weeks after the second vaccination, animals were challenged with a lethal dose of *antigen*-expressing 38C13 lymphoma tumor cells. Animals pre-treated with EDHGF followed by vaccine+*CpG* DNA vaccination had significantly better survival than controls, vaccine treatment alone, or vaccine+*cpG*. These results suggest that in vivo expansion of DC precursors through *administration* of EDHGF augments vaccine potency by increasing *antigen* uptake and *antigen* presentation. Our results represent an important strategy for increasing the effectiveness of vaccination without modification of the *antigen* and without purification of DC.

4/3,K/6 (Item 6 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)
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12980673 BIOSIS NO.: 200100187822

Interleukin-12- and gamma interferon-dependent protection against malaria conferred by CpG oligodeoxynucleotide in mice.

AUTHOR: Gramzinski Robert A; Doolan Denise L; Sedegah Martha; Davis Heather L; Krieg Arthur M; Hoffman Stephen L(a)
AUTHOR ADDRESS: (a)Malaria Program, Naval Medical Research Center, 503 Robert Grant Ave., Silver Spring, MD, 20910-7500: hoffmans@nmrc.navy.mil **USA

JOURNAL: Infection and Immunity 69 (3):p1643-1649 March, 2001
MEDIUM: print
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Unmethylated *CpG* dinucleotides in bacterial DNA or synthetic oligodeoxynucleotides (ODNs) cause B-cell proliferation and immunoglobulin secretion, monocyte cytokine secretion, and activation of natural killer (NK) cell lytic activity and gamma interferon (IFN-gamma) secretion in vivo and in vitro. The potent Th1-like immune activation by *CpG* ODNs suggests a possible utility for enhancing innate immunity against infectious pathogens. We therefore investigated whether the innate immune response could protect against malaria. Treatment of mice with *CpG* ODN 1826 (TCCATGACGTTCCTGACGTT, with the *CpG* dinucleotides underlined) or 1585 (ggGGTCAACGTTGAgggggG, with g representing diester linkages and phosphorothioate linkages being to the right of lowercase

letters) in the absence of *antigen* 1 to 2 *days* prior to challenge with Plasmodium yoelii sporozoites conferred sterile protection against infection. A higher level of protection was consistently induced by *CpG* ODN 1826 compared with *CpG* ODN 1585. The protective effects of both *CpG* ODNs were dependent on interleukin-12, as well as IFN-gamma. Moreover, CD8+ T cells (but not CD4+ T cells), NK cells, and nitric oxide were implicated in the *CpG* ODN 1585-induced protection. These data establish that the protective mechanism induced by *administration* of *CpG* ODN 1585 in the absence of parasite *antigen* is similar in nature to the mechanism induced by immunization with radiation-attenuated P. yoelii sporozoites or with plasmid DNA encoding preerythrocytic-stage P. yoelii *antigens*. We were unable to confirm whether CD8+ T cells, NK cells, or nitric oxide were required for the *CpG* ODN 1826-induced protection, but this may reflect differences in the potency of the ODNs rather than a real difference in the mechanism of action of the two ODNs. This is the first report that stimulation of the innate immune system by *CpG* immunostimulatory motifs can confer sterile protection against malaria.

4/3,K/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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12940575 BIOSIS NO.: 200100147724
Oligonucleotide containing CpG motifs enhances immune response to mucosally or systemically administered tetanus toxoid.
AUTHOR: Eastcott Jean W; Holmberg Cynthia J; Dewhirst Floyd E; Esch Thomas R; Smith Daniel J; Taubman Martin A(a)
AUTHOR ADDRESS: (a)Department of Immunology, Forsyth Institute, 140 Fenway, Boston, MA, 02115: mtaubman@forsyth.org**USA
JOURNAL: Vaccine 19 (13-14):p1636-1642 8 February, 2001
MEDIUM: print
ISSN: 0264-410X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Oligodeoxynucleotides (ODN) containing unmethylated *CpG* dinucleotides induce proliferation of B cells and activation of macrophages and thus stimulation of the immune system. We tested an oligonucleotide containing an unmethylated *CpG* dinucleotide flanked by two 5' purines and two 3' pyrimidines (GAGAACGCTCGACCTTCGAT) for the ability to affect antibody levels to tetanus toxoid (Tt). Groups of male ...

...3) either alone, or with Tt bound to the Al(OH)3, or with Tt bound to Al(OH)3 with the addition of the *CpG* oligonucleotide. *Antigens* were *administered* subcutaneously in the salivary gland vicinity once, or by gastric intubation on 3 consecutive *days*. On *day* 124 all animals were given a boost with the same material by the same route. Serum IgG and saliva IgA antibody to Tt was determined...

...antibody levels were significantly higher in ODN + Tt treated rats than in Tt-alone rats immunized by either route after primary or booster immunizations. Thus, *administration* of an ODN containing unmethylated *CpG* motifs along with an immunogen bound to Al(OH)3 can result in enhanced specific antibody when *administered* by intragastric as well as subcutaneous routes.

4/3,K/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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12020243 BIOSIS NO.: 199900300762

DNA-based immunization for asthma.
AUTHOR: Broide David(a); Raz Eyal
AUTHOR ADDRESS: (a)University of California San Diego, 9500 Gilman Drive, Basic Science Building, Room 5090, La Jol**USA
JOURNAL: International Archives of Allergy and Immunology 118 (2-4):p 453-456 Feb.-April, 1999
ISSN: 1018-2438
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Background: Immunostimulatory DNA sequences (ISS) containing a *CpG* motif are able to inhibit Th2-mediated airway eosinophilia and bronchial hyperresponsiveness in a mouse model of asthma. Methods: To determine the optimal frequency and timing of intervention with ISS in inhibiting Th2 cytokine production and airway eosinophilia, we used ISS *administration* protocols which differed in the frequency (one vs. two doses), route (systemic vs. mucosal) and timing of ISS *administration* (before or together with *antigen*) in a mouse model of ovalbumin-induced eosinophilic airway inflammation. Results: ISS induced Th1 cytokine production (IFN-gamma) and effectively inhibited Th2 cytokine production (IL-5) as well as eosinophilic inflammation when ISS was *administered* before or coadministered with inhaled allergen challenge. Although ISS was effective when coadministered with inhaled allergen, it was most effective when *administered* once 6 *days* prior to allergen challenge. Mucosal (intranasal and intratracheal) delivery of ISS was as effective as systemic (intraperitoneal) ISS delivery in inhibiting airway eosinophilia and switching cytokine responses from a Th2 to a Th1 response. Conclusions: ISS is most effective in inhibiting airway eosinophilia when *administered* as a single dose 6 *days* prior to *antigen* inhalation. However, ISS can also significantly inhibit eosinophilic inflammation, when coadministered with *antigen* inhalation. Thus, ISS *administered* prior or together with allergen should be considered as a novel method of allergen-based immunotherapy.

4/3,K/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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11899588 BIOSIS NO.: 199900145697
Long-lasting anti-metastatic efficiency of interleukin 12-encoding plasmid DNA.
AUTHOR: Schultz Jan; Pavlovic Jovan; Strack Bettina; Nawrath Michael; Moelling Karin(a)
AUTHOR ADDRESS: (a)Inst. Med. Virology, Univ. Zurich, Gloriastrasse 30, CH-8028 Zurich**Switzerland
JOURNAL: Human Gene Therapy 10 (3):p407-417 Feb. 10, 1999
ISSN: 1043-0342
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: antimetastatic activity against lung metastases induced by the malignant melanoma cell line B16-F10. The protective effect of IL-12 DNA is long-lasting, since *administration* of tumor cells 9 *days* after IL-12 DNA treatment prevented metastasis formation. No effects were observed with empty plasmid controls, DNA encoding the melanoma-associated *antigen* pme117/gp100, the granulocyte-macrophage colony-stimulating factor GM-CSF, B7.1, or *CpG*-containing oligodeoxynucleotides. IL-12 DNA is required during early phases of metastasis formation and is ineffective when *administered* later. Its efficiency is dose dependent. The cytotoxic T cell response contributes to the antimetastatic effect as evidenced by genetically modified CD8- or perforin knockout...

4/3,K/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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11812808 BIOSIS NO.: 199900058917
CpG DNA can induce strong Th1 humoral and cell-mediated immune responses against hepatitis B surface antigen in young mice.
AUTHOR: Millan Cynthia L Brazolot; Weeratna Risini; Krieg Arthur M; Siegrist Claire-Anne; Davis Heather L(a)
AUTHOR ADDRESS: (a)Loeb Res. Inst., 725 Parkdale Ave., Ottawa, ON K1Y 4E9** Canada
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 95 (26):p15553-15558 Dec. 22, 1998
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Successful neonatal immunization of humans has proven difficult. We have evaluated *CpG*-containing oligonucleotides as an adjuvant for immunization of young mice (1-14 *days* old) against hepatitis B virus surface *antigen*. The protein-alum-*CpG* formulation, like the DNA vaccine, produced seroconversion of the majority of mice immunized at 3 or 7 *days* of age, compared with 0-10% with the protein-alum or protein-*CpG* formulations. All animals, from neonates to adults, immunized with the protein-alum vaccine exhibited strong T helper (Th) 2-like responses (predominantly IgG1, weak or absent cytotoxic T lymphocytes (CTL)). Th2-type responses also were induced in young mice with protein-*CpG* (in 1-, 3-, and 7-*day*-old mice) and protein-alum-*CpG* (in 1- and 3-*day* -old mice) but immunization carried out at older ages gave mixed Th1/Th2 (Th0) responses. DNA vaccines gave Th0-like responses when *administered* at 1 and 7 *days* of age and Th1-like (predominantly IgG2a and CTL) responses with 14-*day*-old or adult mice. Surprisingly, the protein-alum-*CpG* formulation was better than the DNA vaccine for percentage of seroconversion, speed of appearance, and peak titer of the antibody response, as well as prevalence...

4/3,K/11 (Item 1 from file: 50)
DIALOG(R)File 50:CAB Abstracts
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04314353 CAB Accession Number: 20023151137
Skin-derived macrophages from Leishmania major-susceptible mice exhibit interleukin-12- and interferon- gamma -independent nitric oxide production and parasite killing after treatment with immunostimulatory DNA.
Stebut, E. von; Belkaid, Y.; Nguyen, B.; Wilson, M.; Sacks, D. L.; Udey, M. C.
Department of Dermatology, Johannes Gutenberg-University, Langenbeckstrasse 1, 55131 Mainz, Germany.
Journal of Investigative Dermatology vol. 119 (3): p.621-628
Publication Year: 2002
ISSN: 0022-202X --
Language: English
Document Type: Journal article

--
Co-*administration* of *CpG* -containing immunostimulatory oligodeoxynucleotides and parasite *antigen* protects susceptible BALB/c mice from otherwise progressive infection with Leishmania major. Although the protective effect of *CpG* -containing immunostimulatory oligodeoxynucleotides is clearly dependent on endogenous interleukin-12 and interferon- gamma production, the source of these Th1-promoting cytokines in infected mice is...

... Leishmania-resistant C57BL/6 mice, macrophages from susceptible BALB/c

mice are hyporesponsive to stimulation with lipopolysaccharide and interferon- gamma . While studying interactions of various *antigen* -presenting cells with Leishmania, we found that BALB/c inflammatory skin macrophages, whether Leishmania-infected or uninfected, produced large amounts of interleukin-12 when treated with *CpG* -containing immunostimulatory oligodeoxynucleotides. Like lipopolysaccharide, *CpG* -containing immunostimulatory oligodeoxynucleotides induced production of interferon- gamma and release of nitric oxide by skin macrophages. Studies using skin macrophages from interleukin-12- and interferon...

... and interferon- gamma production. Approximately 44% and 27% of intracellular L. major amastigotes were killed by infected skin macrophages within 72 h upon stimulation with *CpG* -containing immunostimulatory oligodeoxynucleotides and lipopolysaccharide, respectively. Parasite killing by macrophages was independent of endogenous interferon- gamma production, but was strongly enhanced by exogenous interferon- gamma . Parasite elimination was dependent on the induction of nitric oxide, however. In vivo, injection of *CpG*-containing immunostimulatory oligodeoxynucleotides into lesional skin reduced the parasite burden approx equal to 50-fold within the first 5 *days* of infection prior to full generation of a Th response. These results suggest that skin macrophages, constituting the principal reservoir of parasites in infected susceptible mice, produce Th1-promoting cytokines in response to *CpG*-containing immunostimulatory oligodeoxynucleotides. In addition, *CpG* -containing immunostimulatory oligodeoxynucleotides may also act locally on skin macrophages to facilitate Leishmania clearance by inducing nitric oxide production.

4/3,K/12 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
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11645913 99080051 PMID: 9861007

CpG DNA can induce strong Th1 humoral and cell-mediated immune responses against hepatitis B surface antigen in young mice.

Brazolot Millan C L; Weeratna R; Krieg A M; Siegrist C A; Davis H L
Loeb Research Institute, 725 Parkdale Avenue, Ottawa, ON, Canada, K1Y 4E9.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Dec 22 1998, 95 (26) p15553-8, ISSN 0027-8424
Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Successful neonatal immunization of humans has proven difficult. We have evaluated *CpG*-containing oligonucleotides as an adjuvant for immunization of young mice (1-14 *days* old) against hepatitis B virus surface *antigen* . The protein-alum-*CpG* formulation, like the DNA vaccine, produced seroconversion of the majority of mice immunized at 3 or 7 *days* of age, compared with 0-10% with the protein-alum or protein-*CpG* formulations. All animals, from neonates to adults, immunized with the protein-alum vaccine exhibited strong T helper (Th)2-like responses [predominantly IgG1, weak or absent cytotoxic T lymphocytes (CTL)]. Th2-type responses also were induced in young mice with protein-*CpG* (in 1-, 3-, and 7-*day*-old mice) and protein-alum-*CpG* (in 1- and 3-*day* -old mice) but immunization carried out at older ages gave mixed Th1/Th2 (Th0) responses. DNA vaccines gave Th0-like responses when *administered* at 1 and 7 *days* of age and Th1-like (predominantly IgG2a and CTL) responses with 14-*day*-old or adult mice. Surprisingly, the protein-alum-*CpG* formulation was better than the DNA vaccine for percentage of seroconversion, speed of appearance, and peak titer of the antibody response, as well as prevalence...

4/3,K/13 (Item 1 from file: 370)

DIALOG(R)File 370:Science
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00500655 (USE 9 FOR FULLTEXT)
Pycnodysostosis, a Lysosomal Disease Caused by Cathepsin K Deficiency
Gelb, Bruce D.; Shi, Guo-Ping; Chapman, Harold A.; Desnick, Robert J.
B. D. Gelb and R. J. Desnick, Department of Human Genetics and Division of Pediatric Cardiology, Mount Sinai School of Medicine, New York, NY 10029, USA. ; G.-P. Shi and H. A. Chapman, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, USA
Science Vol. 273 5279 pp. 1236
Publication Date: 8-30-1996 (960830) Publication Year: 1996
Document Type: Journal ISSN: 0036-8075
Language: English
Section Heading: Reports
Word Count: 2001

(THIS IS THE FULLTEXT)

...Text: family by exon amplification from genomic DNA and by reverse transcriptase-polymerase chain reaction (RT-PCR) (B9) revealed a C-to-T transversion of a *CpG* dinucleotide at position 343 in the cDNA in both families, predicting an Arg.sup(113) --> Trp (R113W) substitution in the propeptide, near the putative cleavage...be heterozygous for markers across the Pycno critical region. Sequence analysis demonstrated heteroallelism for the G146R mutation and a C-to-T transition of a *CpG* dinucleotide at nucleotide 826, predicting an R241X nonsense mutation. Restriction analysis of amplified segments from genomic DNA with Bam I for G146R and Ava I...

...R241X mutation presumably will be null for cathepsin K activity. The G146R mutation, found in the American Hispanic and Moroccan Arab families, occurred at a *CpG* dinucleotide and may prove to be a common mutation. Because this missense mutation would alter the charge of this residue, which resides near the active...

...K release by osteoclasts or other cells may be injurious. In these common disorders, down-regulation of gene expression by antisense RNA strategies or the *administration* of specific enzyme inhibitors may decrease pathologic bone resorption...together with 3 (mu) g of pAdVAntage (Promega), which contains the adenovirus virus-associated I RNA (VAI) to enhance translation (B20) . Cells were harvested 48 *hours* after transfection and assayed by immunoblotting. Blots were developed with monospecific polyclonal antibodies to human cathepsin K raised by injection of cathepsin K-maltose binding protein fusion protein into rabbits and purified by elution from immobilized *antigen* as described (B21) . Lane 1, nontransfected cells; lanes 2 and 3, 4 and 5, and 6 and 7, cells transfected with 3, 10, or 15...

4/3,K/14 (Item 2 from file: 370)
DIALOG(R)File 370:Science
(c) 1999 AAAS. All rts. reserv.

00500536 (USE 9 FOR FULLTEXT)
Immunostimulatory DNA Sequences Necessary for Effective Intradermal Gene Immunization
Sato, Yukio; Roman, Mark; Tighe, Helen; Lee, Delphine; Corr, Maripat; Nguyen, Minh-Duc; Silverman, Gregg J.; Lotz, Martin; Carson, Dennis A.; Raz, Eyal
Department of Medicine and The Sam and Rose Stein Institute for Research on Aging, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0663, USA.
Science Vol. 273 5273 pp. 352
Publication Date: 7-19-1996 (960719) Publication Year: 1996
Document Type: Journal ISSN: 0036-8075
Language: English
Section Heading: Reports

Word Count: 2127

(THIS IS THE FULLTEXT)

Text: Intramuscular (B1) or intradermal (B2) *administration* of pDNA expression vectors causes intracellular synthesis of the encoded proteins and induction of long-lasting cellular and humoral immune responses. Recently, we reported that...

...by the production of a distinctive cytokine profile [interleukin-2 (IL-2), tumor necrosis factor- (beta) (TNF- (beta)), and, mainly, interferon- (gamma) (IFN- (gamma))] by *antigen*-stimulated CD4 T cells (B6) . The CD4 splenocytes from pACB-Z-immunized mice generated large amounts of IFN- (gamma) and small amounts of IL-4...

...a, IFN- (beta) , and IFN- (gamma) from mouse splenocytes and human peripheral lymphocytes and to enhance natural killer cell activity. These ISS include the following *CpG*-containing hexamers: 5 (prime) -GACGTC-3 (prime) , 5 (prime) -AG-CGCT-3 (prime) , and 5 (prime) -AACGTT-3 (prime) (B7) . Two repeats of 5 (prime...

...that activated adherent splenocytes and enhanced natural killer cell activity in vitro (B9) . Recently, Krieg et al. studied the effects of single-stranded oligonucleotides with *CpG* motifs on murine B lymphocyte activation (B10) . They found that cytosine methylation or the elimination of the *CpG* from the oligonucleotide abolished the lymphocyte stimulatory effect. The activation capability was attributed to a series of *CpG* -containing motifs that generally follow the formula 5 (prime) -Pur Pur CG Pyr Pyr-3 (prime) . *CpG*-enriched oligonucleotides induced not only B cell proliferation, but also the secretion of IL-6 and IFN- (gamma) (B11...

...IL-12. Transfection with pUC19, pACB, pKISS-1-CB, and double-stranded ISS digonucleotide, but not with pKCB or ISS-deficient oligonucleotide, enhanced within 3 *hours* mRNA amounts for all three cytokines (B12) (B13) . IFN-a plays a role in the differentiation of naieve T cells toward a T.inf(H...

...al. showed that the stimulation of IFN- (gamma) synthesis by bacterial DNA is mediated by IL-12 and TNF-a (B20) . Therefore, keratinocytes and dermal *antigen*-presenting cells (APCs) transfected with ISS-containing pDNA could produce IFN-a and IL-12, which would then induce a T.inf(H)1 immune...

...Our findings indicate that immunogenic pDNA may be divided conceptually into two distinct units: a transcription unit that directs *antigen* synthesis and an adjuvant unit in the plasmid backbone that elicits the production of type-1 IFN and IL-12 in the transfected skin keratinocytes and APCs. For this reason, manipulation of the transcription unit within the pDNA to yield higher levels of *antigen* expression does not necessarily produce a stronger immune response. Both the localization and the precise sequence of the ISS within the plasmid backbone are also...

4/3,K/15 (Item 1 from file: 135)
DIALOG(R)File 135:NewsRx Weekly Reports
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0000055368 (USE FORMAT 7 OR 9 FOR FULLTEXT)
CpG Oligonucleotides Generate Antitumor Response In Rodents
Nichols, Sonia
Cancer Weekly, December 11, 2001, p.26

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English
RECORD TYPE: FULLTEXT
WORD COUNT: 444

... rodents, including normal and macrophage depleted Fisher rats, and

nude and SCID mice to perform their analyses of CpG-ODNs and immune system response.

Intermittent *administration* of *CpG*-ODNs to rats with normal macrophage levels up to 19 *days* after they were given subcutaneous inoculations of 9 L glioma cells resulted in significant reductions in tumor volume. In contrast, tumors continued to grow in control rats treated with normal saline. The effect of *CpG*-ODN therapy on tumor inhibition was seen in over a third of the treated rats, Auf and coworkers reported (Implication of macrophages in tumor rejection induced by *CpG* -oligodeoxynucleotides without *antigen*, Clinical Cancer Research , November 2001;7(11):3540-3543).

Tumor-specific long-term protective immunity was also evident, as cured rats rechallenged with injections of...

4/3,K/16 (Item 1 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.
(c) 2003 Thomson Derwent & ISI. All rts. reserv.

0313515 DBR Accession No.: 2003-14655 PATENT

New compositions comprising CpG-containing oligodeoxynucleotides, useful for enhancing Fc receptor-mediated antigen presentation or antibody dependent cellular cytotoxicity, or for treating cancers or bacterial infections - CpG oligonucleotide transfer and expression in host cell for nucleic acid vaccine and gene therapy

AUTHOR: VAN DE WINKEL J G J
PATENT ASSIGNEE: MEDAREX INC 2003

PATENT NUMBER: WO 200325119 PATENT DATE: 20030327 WPI ACCESSION NO.: 2003-354592 (200333)
PRIORITY APPLIC. NO.: US 310437 APPLIC. DATE: 20010803
NATIONAL APPLIC. NO.: WO 2002US24154 APPLIC. DATE: 20020730
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - A composition (I) comprising one or more *CpG* -containing oligodeoxynucleotides in combination with a multispecific molecule that binds to an Fc receptor and a target *antigen* , is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) a vaccine composition comprising one or more *CpG*-containing oligodeoxynucleotides in combination with an Fc receptor (FcR)-targeted *antigen* ; (2) a method of enhancing FcR-mediated antibody dependent cellular cytotoxicity of a target cell comprising *administering* (I) to a subject; (3) a method of inhibiting the growth of a target cell comprising *administering* (I) to a subject; and (4) a method for enhancing FcR-mediated *antigen* presentation comprising *administering* the vaccine composition cited above. BIOTECHNOLOGY - Preferred Composition: The multispecific molecule binds to a human Fcgamma receptor (FcgammaR), preferably FcgammaRI (CD64), FcgammaRII (CD32), or FcgammaRIII (CD16). The multispecific molecule comprises a bispecific antibody. The target *antigen* is a tumor cell or a pathogen. The tumor cell is an ovarian, breast, testicular, prostate, leukemia, or lymphoma tumor cell. The pathogen is a virus or a bacterium. The composition enhances: (a) Fc receptor (FcR)-mediated antibody dependent cellular cytotoxicity (ADCC) of a cell expressing the target *antigen* in the presence of an effector cell; (b) FcR-mediated *antigen* presentation of a cell expressing the target *antigen* ; or (c) dendritic cell-mediated cross-presentation of an FcR-targeted *antigen*. The effector cell is a neutrophil, a monocyte, a macrophage, or a polymorphonuclear cell. The effector cell is preferably a neutrophil, where expression of FcgammaRI (CD64) is upregulated on the neutrophil. The cell is preferably a lymphoma cell, where the composition further comprises a chemotherapeutic agent. The *antigen* in the vaccine composition is a tumor *antigen*, a viral *antigen*, or a bacterial *antigen*. The tumor *antigen* is an ovarian, breast, testicular, prostate, leukemia, or lymphoma tumor *antigen*. The vaccine composition further comprises a chemotherapeutic agent. The FcR is a human FcgammaR, preferably FcgammaRI (CD64), FcgammaRII (CD32), or FcgammaRIII (CD16). The

FcR-targeted *antigen* comprises a fusion protein. The multispecific molecule or the FcgammaR-targeted *antigen* comprises: (a) an antibody, which binds to an FcR at a site that is distinct from the natural ligand binding site of the receptor; (b...

... a single chain antibody; or (c) a human antibody or its fragment. Preferred Method: Enhancing FcR-mediated ADCC of a target cell or FcR-mediated *antigen* presentation further comprises *administering* a chemotherapeutic agent, radiation therapy, or a cytokine. The chemotherapeutic agent is doxorubicin (adriamycin), cisplatin, bleomycin sulfate, carmustine, chlorambucil, or cyclophosphamide hydroxyurea. The cytokine is...

... In enhancing FcR-mediated ADCC of a target cell, the multispecific molecule comprises a bispecific antibody or a human antibody or its fragment. The target *antigen* is a pathogen or a tumor cell, preferably a lymphoma cell. In enhancing FcR-mediated *antigen* presentation, the *antigen* is a tumor *antigen*, a viral *antigen*, or a bacterial *antigen*. The FcR-targeted *antigen* comprises a fusion protein. The composition enhances FcR-mediated *antigen* presentation of a cell expressing the target *antigen*. ACTIVITY - Cytostatic; Virucide; Antibacterial; Immunosuppressive. Groups of 6 C3H/HeN mice were inoculated intraperitoneally with 38C13 T3C tumor cells on *day* 0. The mice were treated once daily (on *days* 5, 7 and 10) with 100 microg monoclonal antibody (mAb; IgG1 or IgG21) alone, 20 microg *CpG* -containing oligodeoxynucleotides (*CpG* ODN) 1826, or a combination. The anti-idiotype murine mAb of the IgG2a and IgG1 isotypes exhibited anti-tumor activity with IgG2a being more effective. *CpG* ODN enhanced the efficacy of anti-tumor IgG2a antibodies in this model. MECHANISM OF ACTION - Vaccine. USE - The compositions are useful for enhancing Fc receptor-mediated *antigen* presentation, antibody dependent cellular cytotoxicity, and other Fc receptor-mediated immune responses. The vaccine composition is useful against tumor *antigen*, viral *antigen* or bacterial *antigen*. The compositions are also useful for treating or preventing diseases, such as cancers, autoimmune diseases, and viral or bacterial infections. *ADMINISTRATION* - *Administration* may be oral, nasal, topical (including buccal or sublingual), rectal, vaginal, or parenteral (including intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous...

4/3,K/17 (Item 2 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.
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0312275 DBR Accession No.: 2003-13415 PATENT

Generating mature dendritic cells for tumor immunotherapy or as vaccines for activating the immune system to treat diseases such as cancer, comprises contacting a dendritic cell precursor with a D type oligodeoxynucleotide - involving vector-mediated gene transfer and expression in host cell for use in cancer therapy

AUTHOR: KLINMAN D M; GURSEL M; VERTHELYI D
PATENT ASSIGNEE: US DEPT HEALTH and HUMAN SERVICES 2003
PATENT NUMBER: WO 200320884 PATENT DATE: 20030313 WPI ACCESSION NO.: 2003-300874 (200329)
PRIORITY APPLIC. NO.: US 312190 APPLIC. DATE: 20010814
NATIONAL APPLIC. NO.: WO 2002US25732 APPLIC. DATE: 20020813
LANGUAGE: English

...ABSTRACT: dendritic cell precursor with an oligodeoxynucleotide of at least 16 nucleotides in length comprising a sequence (I): 5'X1X2X3Pu1Py2CpGPu3Py4X4X5X6(W)M(G)N-3' Central *CpG* motif = unmethylated; Pu = purine nucleotide; Py = pyrimidine nucleotide; X and W = any nucleotide; M = integer 0-10; and N = integer 4-10. INDEPENDENT CLAIMS are also included for the following: (1) a method (M2) for generating an activated T lymphocyte by producing a mature *antigen*

presenting dendritic cell according to (M1), and contacting the mature *antigen* presenting dendritic cell with a T lymphocyte in vitro, producing an activated T lymphocyte; (2) a method (M3) of producing an immune response against an *antigen* in a subject by producing mature *antigen* presenting dendritic cells according to (M1), contacting the mature *antigen* presenting dendritic cell with a T lymphocyte in vitro, and *administering* the activated T lymphocytes to the subject; (3) a single step method (M4) for differentiating a dendritic precursor cell into a mature *antigen*-presenting cell by contacting a dendritic cell precursor with an *antigen* and (I), to differentiate a mature *antigen* presenting cell; and (4) a method (M5) of inducing differentiation of a monocyte by contacting a monocyte and a plasmacytoid dendritic cell with an *antigen* and with (I), inducing the plasmacytoid dendritic cell to produce interferon-alpha inducing the differentiation of the monocyte into a dendritic cell. BIOTECHNOLOGY - Preferred Method: In generating a mature dendritic cell, N is about 6, and Pu Py *CpG* Pu Py comprises phosphodiester bases, where Pu1 Py2 *CpG* Pu3 Py4 are phosphodiester bases. The X1X2X3 and X4X5X6 (W)M(G)N comprise phosphodiester bases or one or more phosphothioate bases. X1X2X3 Pu Py...

... backbone modification. The oligodeoxynucleotide comprises about 100 nucleotides or less, preferably 18-30 nucleotides. The method further comprises contacting the dendritic cell precursor with an *antigen*, where the dendritic cell precursor cell is a monocyte and is in vivo or in vitro. The method further includes contacting the dendritic cell precursor...

... macrophage colony stimulating factor), IL-4 (interleukin 4), flt-3L (FMS-related tyrosine kinase 3 ligand) or a combination of these. Specifically, producing a mature, *antigen*-presenting dendritic cell comprises contacting a dendritic cell precursor with (I), and contacting the dendritic cell precursor with an *antigen* for a time allowing the *antigen* to be presented on the mature dendritic cell, thus producing a mature *antigen*-presenting dendritic cell. The *antigen* is a protein, a polypeptide, a polysaccharide, a DNA molecule, an RNA molecule, a whole cell lysate, an apoptotic cell, or their combinations. The method further comprises contacting the dendritic cell precursor with an agent that enhances dendritic cell maturation. The dendritic cell is contacted with the oligodeoxynucleotide and the *antigen* sequentially or simultaneously. For the single step method of differentiating a dendritic precursor cell into a mature *antigen*-presenting cell, the dendritic precursor cell is not contacted with another mobilization agent. The monocyte and the plasmacytoid dendritic cell are in vivo or in...

... differentiation of the monocyte into a dendritic cell (claimed). The method is useful for generating mature dendritic cells and enhancing T cell responses, thus enhancing *antigen* presentation. Mature dendritic cells are useful for tumor immunotherapy, for augmenting an immune response to an infectious agent or to a vaccine, and as vaccines...

... infection or to activate the immune system to treat diseases such as cancer. Mature dendritic cells may also be used to produce activated T lymphocytes. *ADMINISTRATION* - *Administration* can be local or systemic, by intravenous, intramuscular, intraperitoneal, transmucosal, subcutaneous, transdermal, transnasal, inhalation or oral routes. No dosage given. EXAMPLE - Peripheral blood mononuclear cells and purified elutriated monocytes were cultured in vitro with a variety of D type or control (non-*CpG*) oligodeoxynucleotide (ODN) at an optimized concentration of 3 microM. Phenotypic changes associated with dendritic cell maturation, including increased expression of co-stimulatory molecules, were manifested by 10% monocytes within 24 *hours* of D ODN treatment. By 48 *hours* in culture, a large fraction of monocytes matured into dendritic cells, as characterized by increased surface expression of CD83 and Cd86 but low levels of CD14. Cell yield remained constant while cell viability was equal to or more than 80% after 4

days of culture. (35 pages)

4/3,K/18 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0309880 DBR Accession No.: 2003-11665 PATENT
Epitope having high affinity for major histocompatibility complex class I useful for treating an animal, evaluating immunogenicity of a vaccine or therapeutic composition and for diagnosing a disease - involving virus vector plasmid-mediated gene transfer and expression in dendrite cell for use in recombinant vaccine preparation and disease diagnosis
AUTHOR: SIMARD J J L; DIAMOND D C; LIU L; XIE Z
PATENT ASSIGNEE: CTL IMMUNOTHERAPIES CORP 2003
PATENT NUMBER: WO 2003008537 PATENT DATE: 20030130 WPI ACCESSION NO.: 2003-248010 (200324)
PRIORITY APPLIC. NO.: US 363210 APPLIC. DATE: 20020307
NATIONAL APPLIC. NO.: WO 2002US10189 APPLIC. DATE: 20020329
LANGUAGE: English

...ABSTRACT: physical, biochemical, immunologic, or molecular genetic properties of a molecule embodying the sequence; (14) an isolated polypeptide comprising an epitope cluster from a target-associated *antigen* having the sequence as given in the specification, where the amino acid sequence consists of not more than about 80% of the amino acid sequence of the *antigen* ; (15) an isolated polynucleotide encoding the above polypeptide; and (16) a vaccine or immunotherapeutic product comprising the above polypeptide or polynucleotide. BIOTECHNOLOGY - Preferred Epitope: The...

... acid at an N-terminus of the polypeptide, or a substitution of at least one amino acid. The polypeptide has affinity to an human leukocyte *antigen* (HLA)-A-A2 molecule, where the affinity is determined by an assay of binding, an assay of restriction of epitope recognition, or a prediction algorithm...

...The peptide is an immune epitope or a nucleic acid. (VI) is multivalent. Preferred Composition: In (IX), the adjuvant is a polynucleotide comprising a dinucleotide, *CpG* . The adjuvant is encoded by a polynucleotide. The adjuvant is a cytokine, preferably granulocyte macrophage colony stimulating factor (GM-CSF). (IX) further comprises a professional *antigen*-presenting cell (pAPC), preferably a dendritic cell, and a second epitope which is a polypeptide, a nucleic acid, housekeeping epitope or immune epitope. Preferred Construct...

... Groups of 2 C57BL/6 mice were immunized once with titrated doses (200-0.02 microg) of pEGFPL33A DNA or of control plasmid pEGFP-N3, *administered* intramuscular (i.m.), intradermal (i.d.), intrasplenic (i.spl.), or intra-lymph node (i.ln). Positive control mice received 500 plaque forming unit (pfu) Lymphocytic Choriomeningitis Virus (LCMV) intravenous (i.v.). 10 *days* after immunization induced weakly detectable CTL responses when high doses of pEGFPL33A DNA (200 microg) were *administered* . In contrast, potent gp33-specific CTL responses were elicited by immunization with only 2 microg pEGFPL33A DNA i.spl. and with as little as 0...

...the control pEGFP-N3 DNA did not elicit any detectable gp33-specific CTL responses. USE - (X) is useful for treating an animal. The method comprises *administering* the composition to the animal and assaying to determine a characteristic indicative of a state of a target cell(s). The method comprises a first assaying step preceding the *administering* step and a second assaying step following the *administering* step, comparing the characteristic determined in the first step with second assaying step to obtain a result which includes evidence of an immune response, diminution...

... can be combined with a radiation therapy, chemotherapy, biochemotherapy or surgery. (X) is also useful for evaluating immunogenicity of a vaccine or immunotherapeutic composition, by *administering* the composition to an HLA-transgenic animal and evaluating immunogenicity based on a characteristic of the animal, or by in vitro stimulation (primary stimulation) of... to a step of stimulation with (III). (IV)-(VI), (VIII) are useful for diagnosing a disease. (X) is useful for making a vaccine (all claimed). *ADMINISTRATION* - (X) is *administered* by transdermal, intranodal, perinodal, oral, intravenous, intradermal, intramuscular, intraperitoneal, mucosal route, aerosol inhalation or by instillation (claimed). Dosage details not specified. EXAMPLE - Peptides having the...

4/3,K/19 (Item 4 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.
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0309682 DBR Accession No.: 2003-11467 PATENT

Novel hepatitis C virus E1E2 vaccine composition for stimulating an immune response in a vertebrate, comprises E1E2 antigens, submicron oil-in-water emulsions and/or CpG oligonucleotides - plasmid-mediated gene transfer and expression in CHO cell for use in disease recombinant vaccine and diagnosis

AUTHOR: HOUGHTON M; COATES S R; O'HAGAN D
PATENT ASSIGNEE: CHIRON CORP 2003

PATENT NUMBER: WO 2003002065 PATENT DATE: 20030109 WPI ACCESSION NO.: 2003-247904 (200324)
PRIORITY APPLIC. NO.: US 302227 APPLIC. DATE: 20010629
NATIONAL APPLIC. NO.: WO 2002US20676 APPLIC. DATE: 20020628
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - A composition (I) comprising a hepatitis C virus (HCV) E1E2 *antigen* and a submicron oil-in-water emulsion that lacks N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2- (1'-2'-dipalmitoyl-sn-glycero-3-hydroxyphosphoryloxy)-ethylamine (MTP-PE), where the submicron oil-in-water emulsion is capable of enhancing the immune response to the HCV E1E2 *antigen* and/or an immunostimulatory nucleic acid sequence (ISS), is new. DETAILED DESCRIPTION - A composition (I) comprises a hepatitis C virus (HCV) E1E2 *antigen* and a submicron oil-in-water emulsion that lacks N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2- (1'-2'-dipalmitoyl-sn-glycero-3-hydroxyphosphoryloxy)-ethylamine (MTP-PE), where the submicron oil-in-water emulsion is capable of enhancing the immune response to the HCV E1E2 *antigen* and/or an immunostimulatory nucleic acid sequence (ISS). Alternatively, (I) can be used with ISS alone, without submicron oil-in-water emulsions. An INDEPENDENT CLAIM is also included for making (I), by combining submicron oil-in-water emulsion with HCV E1E2 *antigen*. BIOTECHNOLOGY - Preferred Composition: The HCV E1E2 *antigen* comprises a sequence of amino acids corresponding to positions 192-809 of a sequence of 809 amino acids defined in the specification, or a sequence which has 80% sequence identity to it. (I) further comprises an ISS, preferably a *CpG* oligonucleotide which comprises the sequence GACGTT, GACGTC, GTCGTT or GTCGCT, more preferably 5'-TCCATGACGTTCCTGACGTT-3' or 5'-TCGTCGTTTTGTCGTTTTGTCGTT-3'. The submicron oil-in-water emulsion...

... w/v). ACTIVITY - Virucide. MECHANISM OF ACTION - Vaccine. The immunogenicity of HCV E1E2809 in combination with a submicron oil-in-water emulsion and/or a *CpG* oligonucleotide, was determined. The formulations contained MF59, a submicron oil-in-water emulsion which contained 4-5% w/v squalene, 0.5% weight/volume (w/v) Tween 80 and 0.5% Span 85. The sequence of *CpG* molecule used was 5'-TCGTCGTTTTGTCGTTTTGTCGTT-3'. Chimpanzees were divided into 2 groups (5 animals/group) and *administered* , intramuscularly the vaccine composition. In particular, one group of animals was immunized at 0, 1 and 6 months with 20 microg of E1E2809 and MF59...

... second group of animals was also immunized at 0, 1 and 6 months with 20 microg of E1E2809and MF59, as well as with 500 microg *CpG*. Serum samples were obtained 14 *days* after the last immunization and anti-E1E2 antibody titers determined by enzyme immunoassays. In particular, The E1E2 *antigen* was coated on polystyrene microtiter plates and bound antibody was detected with a horse radish peroxidase (HRP)-conjugated anti-human antibody followed by tetramethylbenzidine substrate development. The results showed that chimpanzees immunized with HCV E1E2 using *CpG* combined with MF59 as adjuvant, produced significantly higher levels of E1E2 antibodies than animals immunized with E1E2 using MF59 alone. USE - (I) is useful for...

... mammal, preferably an anti-E1, anti-E2 and/or anti-E1E2 antibody response and/or a cellular immune response, for either therapeutic or prophylactic purposes. *ADMINISTRATION* - The composition is *administered* at a dose of 0.1 microg-5 mg, by parenteral route, e.g. injection, either subcutaneously or intramuscularly. ADVANTAGE - Use of ISS with or without submicron oil-in-water emulsions provides a safe and effective approach for enhancing immunogenicity of HCV E1E2 *antigens* . EXAMPLE - An hepatitis C virus (HCV) E1E2 complex for use in vaccine compositions was prepared as a fusion protein. Mammalian expression plasmid pMH-E1E2-809...

... by GNA-lectin affinity chromatography. The purified HCV E1E2 was formulated as a vaccine in combination a submicron oil-in-water emulsion (MF59) and a *CpG* oligonucleotide. (69 pages)

4/3,K/20 (Item 5 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0306737 DBR Accession No.: 2003-08522 PATENT
Compositions for treating Th1/Th2 cell-related diseases comprise interleukin-2 or 4 and stromal cell-derived factor-1 alpha, their modulators, modulators of tyrosine kinase Syk, ZAP-70 and nuclear factor of activated T cells - antisense peptide nucleic acid transfer and expression in host cell for gene therapy
AUTHOR: JINQUAN T; POULSEN L K
PATENT ASSIGNEE: ALK-ABELLO AS 2002
PATENT NUMBER: WO 200289832 PATENT DATE: 20021114 WPI ACCESSION NO.: 2003-140201 (200313)
PRIORITY APPLIC. NO.: US 289711 APPLIC. DATE: 20010509
NATIONAL APPLIC. NO.: WO 2002DK295 APPLIC. DATE: 20020507
LANGUAGE: English

...ABSTRACT: compound, peptoid, isothiazolone compound, nocodazole, methyl-3-(N-isothiazolone)-2-thiophenecarboxylate, DNA encoding a catalytically inactive mutant of ZAP-70. IL-2 stimulating adjuvant is *CPG* molecules or MPL (monophosphoryl lipid A). Preferred Nucleic Acid: APNA comprises 5-25, preferably 10-20, more preferably 13-18 bases. ACTIVITY - Immunosuppressive; Cytostatic; Antiallergic...
... and IL-4 double positive were 9.7%, whereas, IFN-gamma or IL-4 single positive were 8.5% or 12.1%, respectively. After 8 *days* of stimulation with IL-2 and SDF-1alpha, the cells were switched to Th1 pattern in terms of expression of IFN-gamma (84%), whereas the...

... such function (data not shown). No significant difference was seen in terms of cellular proliferation between CB CD4+ T cells cultured without stimulus within 8 *days* as detected by (3H)thymidine incorporation into DNA assay. The cells cultured without stimulation had no significant change in terms of expression of intracellular cytokines during 8 *days* (data not shown). CXCR4 (CXC receptor 4) monoclonal antibody (mAb) significantly blocked such on-switch, whereas isotype Ig did not. USE - (C1) and (C2) are...

... eliciting the Th1/Th2-related disease to be treated. In (C1), the pathogenic substance is an infectious agent eliciting an infectious disease, or is an *antigen*, especially an *autoantigen* eliciting an autoimmune disease, or hapten or an allergen eliciting a delayed type hypersensitivity. In (C2) the pathogenic substance is a parasite organism or its portion, an *antigen*, preferably an allergen eliciting an allergic disease Specifically, (C1) is useful for treating or preventing Th1 or Th2 cell-related diseases such as infectious disease ...

... a Th2 cell-related disease such as an allergic disease including hay fever, rhinoconjunctivitis, rhinitis and asthma, and also cancer. (C1) and (C2) are either *administered* to the subject or T helper cells are removed from a subject and contacted ex vivo with the compositions. Treatment may further comprise a second treatment involving the manipulation of the immune system such as vaccination, *antigen* specific immunotherapy, allergen specific immunotherapy, nonspecific immunotherapy or organ transplantation. APNA is useful in the manufacture of a medicament or for preventing or treating a...

... mellitus, autoimmune thyroiditis, hyperthyroidism, cardiovascular diseases such as cardiomyopathy, vasculitis, cardiovascular disease associated with systemic diseases such as systemic lupus erythematosus, scleroderma, and polyarthritis nodosa. *ADMINISTRATION* - *Administration* is oral, parenteral, nasal or pulmonary. Dosage not specified. EXAMPLE - No suitable example given.(77 pages)

4/3,K/21 (Item 6 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0306216 DBR Accession No.: 2003-08001 PATENT

Pharmaceutical composition for treating asthma, has antisense oligonucleotide containing less percentage of adenosine, targeted to nucleic acids associated with lung airway or lung dysfunction, and bronchodilating agent - beta adrenergic agonist transfer and expression in host cell for gene therapy

AUTHOR: NYCE J W; LI Y; SANDRASAGRA A; KATZ E; PABALAN J; AGUILAR D; MILLER S; TANG L; SHAHABUDDIN S
PATENT ASSIGNEE: EPIGENESIS PHARM INC 2002
PATENT NUMBER: WO 200285309 PATENT DATE: 20021031 WPI ACCESSION NO.: 2003-093058 (200308)
PRIORITY APPLIC. NO.: US 286036 APPLIC. DATE: 20010424
NATIONAL APPLIC. NO.: WO 2002US13143 APPLIC. DATE: 20020423
LANGUAGE: English

...ABSTRACT: s)), effective for alleviating bronchoconstriction, respiratory tract inflammation, allergies, and reducing adenosine sensitivity, levels of adenosine (A) or (A) receptors, surfactant depletion or hyposecretion, when *administered* to a mammal. The oligo containing about 1-15% of (A) and being anti-sense to a target comprises: (i) the initiation codon, (ii) the...

... 7-one or 2-amino-6-methoxyaminopurine. In (I), one or more methylated cytosine(s) (mC) are substituted for a C in one or more *CpG* dinucleotide(s), if present in the oligo(s). One or more mononucleotide(s) of (I) are linked or modified by one or more of methylphosphonate... Antiasthmatic; Analgesic; Hypotensive; Immunosuppressive; Cytostatic. MECHANISM OF ACTION - beta Adrenergic Agonist; Antisense therapy. Neonatal New Zealand white Pasteurella-free rabbits were immunized intraperitoneally within 24 *hours* of birth with 312 *antigen* units/ml house dustmite extract mixed with 10% kaolin. Immunizations were repeated weekly for the first month and then biweekly for the next 2 months...

... and measurements of total lung resistance (RL) and dynamic compliance (Cdyn) were calculated at isovolumetric and flow zero points,

respectively. Animals were randomized and on *Day* 1 pretreatment values for PC50 were obtained for aerosolized adenosine. Anti-sense (HAdA1AS) (5'-GATGGAGGGCGGCATGGCGGG-3') or mismatched control (HAdA1MM) oligonucleotides (5'-GTAGCAGGCGGGGATGGGGGC-3') were dissolved in sterile physiological saline at a concentration of 5000 microg (5 mg) per 1.0 ml. Animals were subsequently *administered* the aerosolized anti-sense or mismatch oligonucleotide by the intratracheal tube twice daily for two *days*. Four randomly selected allergic rabbits were *administered* anti-sense oligonucleotide and four the mismatched control oligonucleotide. On the morning of the third *day*, PC50 values (the concentration of aerosolized adenosine in mg/ml required to reduce the dynamic compliance of the bronchial airway 50% from the baseline value...

... either anti-sense or control inhaled oligonucleotide. USE - (I) is useful for preventing or treating a respiratory, lung, or malignant disease or condition which involves *administering* to a subject, preferably a human, simultaneously, sequentially, or separately *administering* (I) and (II). (I) is *administered* for alleviating bronchoconstriction or lung inflammation, or allergies, reducing (A) or (A) receptor levels, or (A) hypersensitivity, or surfactant depletion or hyposecretion. The *administered* composition comprises oligo(s) and is *administered* to reduce the production or availability, or to increase the degradation of the target mRNA or to reduce the amount of target polypeptide present in...

... sequence which is anti-sense to the selected fragment, the second oligonucleotide having an A base content up to and including about 15% (all claimed). *ADMINISTRATION* - (I) and (II) are *administered* into the subject's respiratory system by inhalation, respiration, nasal *administration*, or intrapulmonary *administration*. Preferably, the composition is *administered* directly into the subject's lung(s) or nasally as an aerosol or spray of particle size of about 8-100 micron. The composition is *administered* transdermally or systemically, preferably by oral, intracavitary, intranasal, intraanal, intravaginal, intrauteral, intraarticular, transdermal intrabuccal, intravenous, subcutaneous, intramuscular, intravascular, intratumorous, intraglandular, intraocular, intracranial, intrathecal, intralymphatica l, intraotical, intradermal, intrapulmonary route, or by implantation, inhalation, by slow release, by sustained release or by a pump. (I) and (II) are *administered* topically to the airway, respiratory or pulmonary epithelium of the subject, as an aerosol or spray of liquid or solid powdered particles about 5-10...

4/3,K/22 (Item 7 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0305384 DBR Accession No.: 2003-07169 PATENT
Novel epitopes useful as vaccines, comprises peptides or nucleic acid encoding the peptides, that are useful epitopes of target-associated antigens - plasmid-mediated gene transfer and expression in host cell for disease gene therapy and nucleic acid vaccine
AUTHOR: SIMARD J J L; DIAMOND D C; LIU L; XIE Z
PATENT ASSIGNEE: CTL IMMUNOTHERAPIES CORP 2002
PATENT NUMBER: WO 200281646 PATENT DATE: 20021017 WPI ACCESSION NO.: 2003-067518 (200306)
PRIORITY APPLIC. NO.: US 363210 APPLIC. DATE: 20020307
NATIONAL APPLIC. NO.: WO 2002US11101 APPLIC. DATE: 20020404
LANGUAGE: English

...ABSTRACT: biochemical, immunologic, or molecular genetic properties of a molecule embodying the sequence; (15) an isolated polypeptide (VIII) comprising an epitope cluster from a target-associated *antigen* having the sequence as disclosed in the specification, where the amino acid sequence consists of not more than 80 % of the amino acid sequence of

the *antigen*; (16) a vaccine or immunotherapeutic product comprising (VIII); (17) an isolated polynucleotide (IX) encoding (VIII); and (18) a vaccine or immunotherapeutic product comprising (IX). WIDER...

...similarity comprises addition or substitution of at least one amino acid at an N-terminus of the polypeptide. (P) has affinity to a human leukocyte *antigen* (HLA)-A2, HLA-B7 or HLA-B51 molecule, as determined by an assay of binding, an assay of epitope recognition, or by a prediction algorithm...

... cell, a bacterium, fungus or protozoan. Preferred Protein: (V) is multivalent. Preferred Composition: In PC the adjuvant is a polynucleotide comprising a dinucleotide such as *CpG*, or is encoded by a polynucleotide, preferably a cytokine such as granulocyte macrophage-colony stimulating factor (GM-CSF). PC further comprises a professional *antigen*-presenting cell (pAPC) which is a dendritic cell and a second epitope is a polypeptide, nucleic acid, a housekeeping or immune epitope. ACTIVITY - Cytostatic. The elicitation of anti-tumor immunity by intra-lymph node DNA immunization was studies. Groups of 6 C57BL/6mice were immunized three times at 6-*day* intervals with 10 micro-g of pEFGPL33A DNA (DNA vaccine containing a immunodominant cytotoxic T-lymphocyte (CTL) epitope from the LCMV-glycoprotein gp33) or control pEGFP-N3 DNA. 5 *days* after the last immunization small pieces of solid tumors expressing the gp33 epitope (EL4-33) were transplanted subcutaneously into both flanks and tumor growth was measured every 3-4 *days*. Although the EL4-33 tumors grew well in mice that had been repetitively immunized with control pEGFP-N3 DNA, mice which were immunized with pEFGPL33A DNA i.ln. rapidly eradicated the peripheral EL4-33 tumors. MECHANISM OF ACTION - Vaccine. USE - VC is useful for treating an animal, by *administering* to an animal the vaccine or immunotherapeutic composition. The method further comprises assaying to determine a characteristic indicative of a state of a target cells. A first assaying step precedes the *administering* step and the second assaying step follows the *administering* step. The method further comprises comparing the characteristic determined in the first assaying step with the characteristic determined in the second assaying step to obtain therapy, chemotherapy, biochemotherapy and surgery. VC is also useful for evaluating immunogenicity of a vaccine or immunotherapeutic composition, by *administering* VC to an HLA-transgenic animal and evaluating immunogenicity based on a characteristic of the animal, or by in vitro primary stimulation of a T ...

... III), (IV), (V) or (VII) is useful for diagnosing a disease. (I), (II), PC, (IV) or (VII) is useful for making a vaccine. (All claimed.) *ADMINISTRATION* - *Administered* by transdermal, intranodal, perinodal, oral, intravenous, intradermal, intramuscular, intraperitoneal, mucosal, aerosol inhalation and instillation (claimed). No dosage is given. EXAMPLE - No relevant examples are given ...

4/3,K/23 (Item 8 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.
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0303582 DBR Accession No.: 2003-05367 PATENT

New isolated proteins capable of raising antibodies in humans, useful for treating interleukin-13 mediated diseases, e.g. asthma, allergies, helminth-infection related disorders, fibrosis or cirrhosis of the liver - vector plasmid pGEX4T3-cIL-13-mediated gene transfer and expression in Escherichia coli for use in gene therapy, recombinant vaccine and nucleic acid vaccine preparation

AUTHOR: ASHMAN C; CROWE J S; ELLIS J H; LEWIS A P

PATENT ASSIGNEE: GLAXO GROUP LTD 2002

PATENT NUMBER: WO 200270711 PATENT DATE: 20020912 WPI ACCESSION NO.: 2002-740766 (200280)

PRIORITY APPLIC. NO.: GB 20015360 APPLIC. DATE: 20010303

NATIONAL APPLIC. NO.: WO 2002GB900 APPLIC. DATE: 20020301
LANGUAGE: English

...ABSTRACT: and (c) is not an antibody. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a protein having B-cell epitopes from a mammalian self *antigen* and a mutation that gives rise to a sequence of an analogous protein of a second mammalian species (the protein is able to raise in...
... the protein, polynucleotide, vector cited above, and a carrier or excipient; (9) a method for the treatment or prophylaxis of IL-13 mediated disease comprising *administration* of the composition in (8) in patient; and (10) a method for preparing the protein. WIDER DISCLOSURE - Also disclosed includes a vaccine composition the polypeptide...

... additionally comprises an adjuvant. It further comprises the protein cited above and an immunostimulatory oligonucleotide selected from: (a) TCC ATG ACG TTC CTG ACG TT (*CpG* 1826) (OLIGO 1); (b) TCT CCC AGC GTG CGC CAT (*CpG* 1758) (OLIGO 2); (c) ACC GAT GAC GTC GCC GGT GAC GGC ACC ACG (OLIGO 3); (d) TCG TCG TTT TGT CGT TTT GTC GTT (*CpG* 2006) (OLIGO 4); or (e) TCC ATG ACG TTC CTG ATG CT (*CpG* 1668) (OLIGO 5). Preferred Method: Preparing a the protein comprises: (a) identification of one or more regions of a self-typically human, protein against which...

... pulmonary disease (COPD), or allergies. The polypeptides or the polynucleotides are useful for the treating helminth-infection related disorders, fibrosis or cirrhosis of the liver. *ADMINISTRATION* - The dosage of the nucleic acid is 50 microg-1 mg if directly *administered* , while 0.5-5 microg/kg if comprised in the vaccine. For the protein, the dosage is 1-1000 (preferably 1-50) microg/dose. The vaccine can be *administered* via the mucosal (such as ...GST-cIL-13 was induced by adding 0.5 mM isopropyl-beta-D-thiogalactopyranoside (IPTG) to a culture in the logarithmic growth phase for 4 *hours* at 37degreesC. The bacteria were than harvested by centrifugation and GST-cIL-13 was purified by glutathione sepharose affinity chromatography.(83 pages)

4/3,K/24 (Item 9 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0302481 DBR Accession No.: 2003-04266 PATENT
New compositions comprising CpG-like immunostimulatory nucleic acids, useful for treating or preventing infectious diseases, cancer, allergy, asthma, immunodeficiency, anemia, thrombocytopenia or neutropenia - oligonucleotide transfer and expression in host cell for immunostimulant and gene therapy
AUTHOR: SCHETTER C; VOLLMER J
PATENT ASSIGNEE: COLEY PHARM GROUP LTD 2002
PATENT NUMBER: WO 200269369 PATENT DATE: 20020906 WPI ACCESSION NO.: 2002-723213 (200278)
PRIORITY APPLIC. NO.: US 254341 APPLIC. DATE: 20001208
NATIONAL APPLIC. NO.: WO 2001IB2888 APPLIC. DATE: 20011210
LANGUAGE: English

...ABSTRACT: cytosine; I = inosine; and X1, X2, X3 and X4 = nucleotides. An INDEPENDENT CLAIM is also included for a method for inducing an immune response by *administering* to a subject the novel composition. BIOTECHNOLOGY - Preferred Composition: The immunostimulatory nucleic acid comprising (I) preferably has a sequence that includes the formula (Ia). The...
... acid is 18 nucleotides long and is not an antisense nucleic acid. The pharmaceutical carrier is a sustained-release device. The composition further comprises an *antigen* , an anti-cancer medicament (e.g. a monoclonal antibody, a chemotherapeutic agent or a radiotherapeutic agent), an antiviral agent, an antibacterial agent, an antifungal agent ...

... granulocyte-macrophage colony-stimulating factor (GM-CSF)). Preferably, the composition includes at least two immunostimulatory nucleic acids having different sequences. The composition further comprises a *CpG* nucleic acid having at least one unmethylated *CpG* motif. Preferred Method: Inducing an immune response in a subject further comprises *administering* the *antigen* (e.g. an allergen, a tumor *antigen*, a viral *antigen*, a bacterial *antigen*, a fungal *antigen* or a parasitic *antigen*), or the anti-cancer therapy. The immunostimulatory nucleic acid is *administered* in an amount for stimulating natural killer cell activity. ACTIVITY - Antimicrobial; Cytostatic; Antiallergic; Antiasthmatic; Immunostimulant; Antianemic; Hemostatic. MECHANISM OF ACTION - Interleukin-Inducer-1-Beta; Interleukin...

... Inducer-Alpha; Interferon-Inducer-Gamma. Peripheral blood monocytes (PBMC) (3x10 to the power 6 cells/ml) obtained from several blood donors were incubated for 8 *hours* with 6 micro-g/ml of the composition containing oligodeoxynucleotide (ODN) 2006, 2117, 2137, or 1 micro-g/ml lipopolysaccharide (LPS) as positive control. Negative controls were similarly incubated for 8 *hours* in the absence of added ODN or LPS. After 8 *hours*, supernatants were collected and IL-1beta (which plays a role in the stimulation of B, T and NK cells, and participates in the conversion of Langerhans cells to professional *antigen*-presenting dendritic cells, and acts as a chemoattractant for leukocytes) was measured by enzyme linked immunosorbent assay (ELISA). Results showed that *CpG* ODN were potent inducers of IL-beta secretion. USE - The compositions are useful for inducing an immune response in a subject, e.g. dog, cat...

... interleukin (IL)-1beta, IL-2, IL-6, IL-12, IL-18, tumor necrosis factor (TNF)-alpha, interferon (IFN)-alpha or IFN-gamma) production. (All claimed). *ADMINISTRATION* - *Administration* is by mucosal route (e.g. oral, nasal, rectal, vaginal, transdermal or ocular) or parenteral route (e.g. intravenous, subcutaneous, intramuscular or direct injection), or in a sustained-release vehicle (claimed). For mucosal delivery, dosage is 0.1 micro-g-10 mg, preferably 100 micro-g-1 mg/*administration*, with 2-4 *administration* spaced *days* or weeks apart. For parenteral *administration* , dosage is 10 micro-g-5 mg, preferably 100 micro-g-1 mg/*administration*, with 2-4 *administrations* spaced *days* or weeks apart. EXAMPLE - No relevant example given. (148 pages)

4/3,K/25 (Item 10 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0302373 DBR Accession No.: 2003-04158 PATENT
Inducing or enhancing antigen specific T cell responses, for preparing a medicament for treating (myco)bacterial disease, a viral disease and cancer, comprises using a peptide with a T cell epitope specific for the antigen - vaccine preparation useful for bacterium infection, virus infection and cancer therapy
AUTHOR: VAN DER BURG S H; OTTENHOF T H M; GELUK A; SCHOENMAEKERS-WELTERS M J P; DE JONG A M; OFFRINGA R; MELIEF C J M; TOES R E M
PATENT ASSIGNEE: ACAD ZIEKENHUIS LEIDEN 2002
PATENT NUMBER: WO 200270006 PATENT DATE: 20020912 WPI ACCESSION NO.: 2002-713424 (200277)
PRIORITY APPLIC. NO.: EP 2001203298 APPLIC. DATE: 20010831
NATIONAL APPLIC. NO.: WO 2001NL893 APPLIC. DATE: 20011207
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - Inducing and/or enhancing an *antigen* specific T cell response, comprising providing a system capable of exhibiting the response with a peptide comprising a T cell epitope specific for the *antigen*, is new. The peptide comprises 22-45 amino-acid residues. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also

included for: (1) a peptide comprising 22-45 amino acid residues having a T cell epitope specific for an *antigen*; (2) a method for obtaining an *antigen* specific T cell, comprising inducing and/or enhancing a T cell response specific for the *antigen*, and collecting the *antigen* specific T cell from the system; (3) an isolated T cell obtained by the method of (2); (4) a medicament comprising the peptide of (1...

... and/or enhancing HPV16 E7 protein-specific, and/or HPV16 E6 protein-specific, and/or HPV16 E2 protein-specific immune response in an individual by *administering* to the individual the peptide of (6) and/or the T-cell of (9); (11) vaccines comprising the peptide of (1) or (6); and (12...

... and (c) detecting any bound IFNgamma. BIOTECHNOLOGY - Preferred Method: The peptide comprises: (a) 22-40 ammo acid residues; (b) a sequence capable of activating an *antigen* presenting cell; (c) a T helper activating sequence; (d) at least two T cell epitopes for the *antigen* ; or (e) at least one T-helper cell epitope for the *antigen* and at least one cytotoxic T lymphocyte (CTL) epitope for the *antigen*. Upon providing the peptide, it is processed by an *antigen*-presenting cell. At least one of the epitopes comprises a T-helper cell epitope for the *antigen* or a CTL epitope for the *antigen*. The *antigen* comprises: (i) a viral protein or an immunogenic part, its derivative and/or analogue, preferably HPV protein, where the protein comprises E2, E6 and/or E7; (ii) an auto-*antigen*, preferably a tumor cell specific auto-*antigen* or a functional part, its derivative and/or analogue; or (iii) a viral or (Myco)bacterial *antigen*, preferably Mycobacterium tuberculosis and Mycobacterium leprae hsp65 369-412. Immunizing with a peptide comprising 21 amino acids or less induces tolerance and/or functional deletion of *antigen* specific CTL in the system. The method further comprises providing the system with an adjuvant comprising an exosome, a dendritic cell, monophosphoryl lipid A and/or *CpG* nucleic acid. The system comprises an animal or a human, where the animal is suffering from or at risk of suffering from a disease, e...

... HPLC-purified 32-amino acid long peptide (A2) () containing this CTL epitope. Mice were vaccinated subcutaneously with peptide in a volume of 200 microliters at *day* 1. Fourteen *days* later mice were challenged with 0.5 x 106 AR5 tumor cell. Survival of mice was monitored during a 100-*day* follow-up. Results show that immunization with synthetic peptides of the exact CTL epitope length can lead to CTL tolerance associated with the inability to reject tumors. The control mice (n = 8) that was vaccinated with the exact peptide-epitope (A1) all die within 50 *days* after tumor challenge. In contrast, the group of mice vaccinated with the 32-amino acid long peptide all live at 50 *days* and only one mouse is lost during the 100-*day* follow-up. Ser-Gly-Pro-Ser-Asn-Thr-Pro-Pro-Glu-Ile (A1) Arg-Glu-Cys-Asn-Ser-Ser-Th r-Asp-Ser-Cys-Asp-Ser...

... Lys-Pro (A2) MECHANISM OF ACTION - Vaccine; Interferon Gamma. USE - The peptide is useful for inducing and/or enhancing an immune response specific for an *antigen* and for preparing a vaccine for treating and/or preventing HPV-related disease. The vaccine or T cell is useful for treating a subject with...

... from a (myco)bacterial disease, a viral disease and/or cancer. The peptide can be used to determine if a collection of cells comprises an *antigen* specific T cell, where the peptide comprises an epitope for the *antigen*, and for determining if an individual comprises immunity for the *antigen*. The T cell can also be used for immunotherapy (all claimed). EXAMPLE - PBMC (Peripheral blood mononuclear cells) or cord blood cells (CBC) were seeded at...

...pools of influenza A/PR/8/34 M1 protein derived peptides consisting of 4 overlapping 30 amino acid long peptides in each pool. A 4-*day* stimulation was used before PBMC were transferred to the ELISPOT plates. This resulted in a pronounced IFNgamma-production towards

influenza M1-derived peptides in the...

4/3,K/26 (Item 11 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0301805 DBR Accession No.: 2003-03590 PATENT
Activating a dendritic cell for cancer immunotherapy or for treating infectious or allergy disease, by contacting a dendritic cell with an isolated nucleic acid containing at least one unmethylated CpG dinucleotide - oligonucleotide transfer and expression in host cell for gene therapy
AUTHOR: KRIEG A M; HARTMANN G
PATENT ASSIGNEE: UNIV IOWA RES FOUND 2002
PATENT NUMBER: US 6429199 PATENT DATE: 20020806 WPI ACCESSION NO.: 2002-689667 (200274)
PRIORITY APPLIC. NO.: US 191170 APPLIC. DATE: 19981113
NATIONAL APPLIC. NO.: US 191170 APPLIC. DATE: 19981113
LANGUAGE: English

...ABSTRACT: NOVELTY - Activating (M) or causing maturation of a dendritic cell, comprising contacting a dendritic cell with an isolated nucleic acid containing at least one unmethylated *CpG* dinucleotide, where the nucleic acid is from 8-80 bases in length in an amount effective to activate or cause maturation of the dendritic cell...

... of the nucleic acid. The isolated nucleic acid has a sequence selected from TCGTCGTTTTGTCGTTTTGTCGTT and TCGTCGTTGTCGTTTTGTCGTT. (M) further comprises contacting the dendritic cell with an *antigen* prior to the isolated nucleic acid or contacting the dendritic cell within 48 *hours*, preferably 24 *hours* of contacting the dendritic cell with the isolated nucleic acid. ACTIVITY - Cytostatic; Antiallergic. MECHANISM OF ACTION - Activator of dendritic cells (claimed); Inducer of dendritic cell maturation. Mature human dendritic cell (DC) expressed the specific DC marker CD83, while immature DC do not. Mature DC effectively presented *antigen* and maintained their stimulatory capacity while migrating from peripheral tissues to lymph nodes. Maturation of DC was thought to be essential if these cells were intended to be used for therapeutic strategies where they would be activated ex vivo, pulsed with *antigens*, and then reinfused into a patient. Freshly isolated DC were incubated for 3 *days* with granulocyte macrophage-colony stimulating factor (GM-CSF), lipopolysaccharide (LPS) or oligonucleotides. The results showed that in the absence of either GM-CSF or *CpG*, or with the methylated control oligonucleotide 2117: 5'-TQGTQGTTTTGTQGTTTTGTQGTT-3' (2 microg/ml), survival of cells was poor. The remaining viable cells did not express...

...was present in addition to GM-CSF, the percentage of CD83 positive cells was increased to 8.6 %. In contrast, the single addition of the *CpG* oligonucleotide 2006: 5'-TCGTCGTTTTGTCGTTTTGTCGTT-3' rendered 16 % of the DC CD83 positive. The combination of GM-CSF and 2006 enhanced CD83 expression synergistically (37 %). This induction of CD83 expression was *CpG* specific as showed by the control oligonucleotide 2117 in combination with GM-CSF (9.7 %). USE - (M) is useful for cancer immunotherapy or for treating an infectious disease or allergy, by *administering* an activated dendritic cell that express a specific cancer, microbial or allergy causing *antigen*, to a subject having a cancer including the cancer *antigen*, to a subject having an infection with a microorganism including the microbial *antigen* or to a subject having an allergic reaction to the allergy causing *antigen*, where the activated dendritic cell is prepared by (M). (M) is useful for generating a high yield of dendritic cells by *administering* an isolated nucleic acid containing at least one unmethylated *CpG* dinucleotide, where the nucleic acid is 8-80 bases in length in an amount effective to activate the dendritic cells to a subject, and

isolating dendritic cells from the subject. (All claimed). *ADMINISTRATION* - The isolated nucleic acid is *administered* by oral, transdermal, subcutaneous, intravenous, parenteral, intraperitoneal or intrathecal route. No dosage is given. ADVANTAGE - The use of *CpG* allows the generation of mature dendritic cells from peripheral blood within two *days* in a well defined system. The application of *CpG* for this purpose is superior to granulocyte macrophage-colony stimulating factor (GM-CSF), which is currently used for this purpose. *CpG* oligonucleotides have a longer half life, are less expensive, and show a greater magnitude of immune effects. EXAMPLE - No relevant example is given.(52 pages)

4/3,K/27 (Item 12 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0300965 DBR Accession No.: 2003-02749 PATENT
Novel Helicobacter proteins, HP30 and HP56, and nucleic acids encoding the proteins, useful as vaccines for raising immune response in animals - vector plasmid-mediated gene transfer and expression in host cell for use in recombinant vaccine preparation and cancer diagnosis, prevention and therapy
AUTHOR: TIAN J; WALKER R; JACKSON W J
PATENT ASSIGNEE: ANTEX BIOLOGICS INC 2002
PATENT NUMBER: WO 200251237 PATENT DATE: 20020704 WPI ACCESSION NO.: 2002-666854 (200271)
PRIORITY APPLIC. NO.: US 732091 APPLIC. DATE: 20001207
NATIONAL APPLIC. NO.: WO 2001US48392 APPLIC. DATE: 20011207
LANGUAGE: English

...ABSTRACT: the specification, with the proviso that the peptides are arranged in a configuration that is different from naturally occurring configuration; (3) antibody (Ab) or its *antigen*-binding fragment that specifically binds to (I), (Ia) or a fragment comprising S4; (4) vaccine composition (VC) comprising (I), (Ia), (Ib) or (Ab), and a...

... composition (PC) comprising (II); (7) vaccine (III) comprising (I) or (II), and one or more adjuvants or immunostimulatory compounds selected from alum, mLT, QS21, MF59, *CpG*, DNA, PML, calcium phosphate, calcium sulfate dihydrate, PLG, CT, LTB and CT/LT, where the compounds may be the same or different; (8) plasmid (P1...

... presence of (II) or (I) in a test sample; (4) agonists of (I) or (II); (5) chimeric or humanized antibodies; (6) antisera raised against the *antigenic* or immunogenic composition comprising (I) or (II); and (7) T-cells specific for Helicobacter or *antigen* presenting cell displaying Helicobacter *antigens*. BIOTECHNOLOGY - Preparation: (I) is produced by culturing (V) under conditions suitable for expression of the HP30 or HP56 polypeptide, and recovering the HP3 or HP56...

... 5 ml 5% sodium bicarbonate followed 10 minutes later with 0.25 ml of vaccine with or without adjuvant in phosphate buffered saline (PBS), at *days* 0, 14 and 28. Two weeks after the last vaccination (therapeutic), mice were challenged by intragastric inoculation of one dose of 107 H.felis or 3 doses of 108 H.pylori within a 5 *day* period. For therapeutic studies, mice were first colonized (*Day* 0) with H.felis or H.pylori and then orally vaccinated on *Days* 21, 35 and 49 after challenge. Two weeks after challenge (prophylactic) or after the last vaccination (therapeutic), mice were euthanized with CO2 and the longitudinal...at lower levels than mice immunized with crude H.pylori cell lysate. The results also demonstrated that the protective efficacy of the HP30 and HP56 *antigens* can be achieved with or without the co-*administration* of the adjuvant. USE - (I), (Ia), (Ib), (II), (III) or VC are useful for producing an immune response in an animal, where (III) or VC is *administered* sequentially or simultaneously. (I), (Ia), (Ib), VC or (III) is useful for preventing, treating or

ameliorating a disorder or disease associated with infection of an animal with Helicobacter, where an antibiotic with Helicobacter bactericidal activity is *administered* prior to, simultaneously with, or sequentially to *administration* of the vaccine (claimed). One or more antibiotics are selected from meprazole, clarithromycin, omeprazole, metronidazole, tetracycline, Lansoprazole and amoxicillin. (I) or (II) is useful for...

... diagnostic, prophylactic or therapeutic agents, and in standard immunoassays to screen for the presence of Ab or T cells to Helicobacter in a biological sample. *ADMINISTRATION* - 0.1-100 mg, preferably 0.5-25 mg of (III) is *administered* through ocular, intranasal, pulmonary, oral, intestinal, rectal, vaginal, urinary track surface or parenteral route. EXAMPLE - Polymerase chain reaction (PCR) was employed to generate Helicobacter protein...

4/3,K/28 (Item 13 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.
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0298018 DBR Accession No.: 2002-19865 PATENT

CYP1B1 polynucleotide for inducing immune response against cancer, has transcriptional units encoding polypeptides, and lack sequences found in untranslated region of naturally occurring forms of transcript - vector-mediated cytochrome-P450 gene transfer and expression in host cell for nucleic acid vaccine and gene therapy

AUTHOR: AZIZ N; HEDLEY M L; URBAN R G; TOMLINSON A J; COLE G

PATENT ASSIGNEE: ZYCOS INC 2002
PATENT NUMBER: WO 200242325 PATENT DATE: 20020530 WPI ACCESSION NO.: 2002-557504 (200259)
PRIORITY APPLIC. NO.: US 298428 APPLIC. DATE: 20010615
NATIONAL APPLIC. NO.: WO 2001US45170 APPLIC. DATE: 20011031
LANGUAGE: English

...ABSTRACT: and third segments are non-contiguous portion of CYP1B1, and first segment comprises the sequence (S1). Preferred Composition: In C1, the immunostimulatory agent is a *CpG* containing oligonucleotide of 18-30 nucleotides, and is preferably interleukin (IL)-12, interferon (IFN)-gamma or a bacterial polypeptide, or is a lipid, nucleic acid...

... which encodes a protein that is processed, presented and can stimulate major histocompatibility complex (MHC) class II CD4+ T cell response. Mice were boosted on *day* 14 with the same dose of pcDNA3-hulB1. Spleens were harvested on *day* 27 and IFN-g ELISPOT assays were performed using CD4+T cell enriched splenocytes tested against syngeneic *antigen* presenting cell (APC) pulsed with peptide. In addition, CD4+T cells isolated from naive mice were screened to serve as a negative control. All CD4...

... mammal suffering from or is at risk for cancer, where the method preferably comprises detecting expression of CYP1B1 in a tumor of a mammal, and *administering* (I), where the mammal belongs to a species especially human, and CYP1B1 or its portion is identical to a sequence of a naturally occurring CYP1B1...

...a rat or mouse. (I) is further useful for reducing tumor growth or tumor activity in a mammal by identifying a mammal having a tumor, *administering* (I), and detecting a reduction in the size or activity of the tumor (claimed). *ADMINISTRATION* - (I) is *administered* subcutaneously or intramuscularly (claimed), or intravenously, intraarterially, intradermally, intraperitoneally, intranasally, intravaginally or intrarectally. Dosage of (I) is 10-1000 microg. EXAMPLE - cDNAs encoding human CYPIBI...

4/3,K/29 (Item 14 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.
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0296262 DBR Accession No.: 2002-18109 PATENT

Adjuvant composition useful in vaccine composition for use in medicine, comprises combination of immunostimulatory oligonucleotide and tocol - adjuvant composition, oil and water emulsion and delivery system for bacterium, virus and parasitic infection vaccine and immunotherapy

AUTHOR: GARCON N; GERARD C M G; STEPHENNE J
PATENT ASSIGNEE: SMITHKLINE BEECHAM BIOLOGICALS 2002
PATENT NUMBER: WO 200232454 PATENT DATE: 20020425 WPI ACCESSION NO.: 2002-499992 (200253)
PRIORITY APPLIC. NO.: GB 200025577 APPLIC. DATE: 20001018
NATIONAL APPLIC. NO.: WO 2001EP11985 APPLIC. DATE: 20011016
LANGUAGE: English

...ABSTRACT: oligonucleotide (Ia) and a tocol (Ib), is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a vaccine composition (II) comprising (I), and an *antigen* or *antigenic* composition; (2) shifting (M1) the quality of an immune response against an *antigen* , generated by a vaccine comprising an immunostimulatory oligonucleotide, towards a Th1-type immune response, by formulating the vaccine with (Ia) and (Ib); and (3) manufacturing...
... oil in water emulsion comprising a tocol, admixing the tocol emulsion with an immunostimulatory oligonucleotide to form an adjuvant, and formulating the adjuvant with an *antigen* or *antigenic* composition. WIDER DISCLOSURE - The following are disclosed: (1) a delivery device for systemic *administration* , pre-filled with (I) or (II); and (2) formulations comprising protease protein fusions based on protease protein, their fragments or homologs. BIOTECHNOLOGY - Preferred Composition: (Ib...

... or double bond; and n = 1-10. (I) further comprises an additional immunostimulant e.g. lipopolysaccharides or its derivative, 3D-MPL, saporin or QS21. The *antigen* in (II) is extracellular domain of Her2Neu linked to the phosphorylation domain (ECD-PD). Preferred Method: The combination of (Ib) with (Ia) containing oil in water emulsion generates a Th1-type immune response such that when *antigen* specific IgG isotypes induced by the vaccine after vaccination of a mouse are measured, IgG1 constitutes less than 50% of the total *antigen* specific IgG as determined by mid point titres measured by isotope specific Enzyme Linked Immunosorbent Assay (ELISA). ACTIVITY - Antiallergic; Antibacterial; Antifungal; Virucide; Cytostatic; Antiarteriosclerotic; Nootropic; Neuroprotective; Anti-HIV; Tuberculostatic; Hepatotropic. MECHANISM OF ACTION - Vaccine (claimed). A range of adjuvant formulations with *antigen* (a fusion of the extracellular domain of Her2Neu linked to the phosphorylation domain (ECD-PD) were investigated. Groups 1-11 were treated with adjuvant formulations comprising the following 11 adjuvants and 25 microg of *antigen* . The adjuvants include phosphate buffered saline (PBS); liposomes with QS21 and 3D-MPL in membrane; tocol containing oil in water emulsion with QS21 and 3D-MPL; *CpG*; liposomes with QS21 and 3D-MPL in membrane + *CpG*; tocol containing oil in water emulsion with QS21 and 3D-MPL + *CpG*; 3D-MPL + *CpG*; QS21 + *CpG*; tocol containing oil in water emulsion + *CpG*; liposomes with QS21 in membrane + *CpG*; and liposomes with 3D-MPL in membrane + *CpG*. Groups of B6F1 mice were vaccinated on four occasions, intramuscularly, 14 *days* apart. Fourteen *days* post the 4th vaccine dose, the mice were challenged subcutaneously with 2 x 10 to the power of 6 TC1 tumor cell expressing the Her2Neu...

... size of the individual tumors were measured twice a week and expressed as a group mean. The results were shown graphically. Formulations comprising tocol and *CpG* induced a complete regression of the tumor. USE - (II) is useful for treating an individual susceptible to or suffering from a disease, and in medicine...
... Alzheimer's disease, and persistent infections. (II) is particularly

suitable for the immunotherapy of infectious diseases such as tuberculosis, AIDS and hepatitis B virus infections. *ADMINISTRATION* - (I) is *administered* through systemic or mucosal route. (I) or (II) is also *administered* through oral, parenteral, intravenous, intradermal, transdermal, intranasal or intramuscular route. Dosage is 1-1000 microg, preferably 1-50 microg. EXAMPLE - None given. (42 pages)

4/3,K/30 (Item 15 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0295021 DBR Accession No.: 2002-16868 PATENT
Immunogenic composition useful for treating patients suffering from cancer comprising cancer antigens e.g., MAGE, prostase, along with adjuvant combination comprising immunostimulatory oligonucleotide and saponin - vaccine for allergy, autoimmune disease and cancer immunotherapy
AUTHOR: GARCON N; GERARD C M G; STEPHENNE J
PATENT ASSIGNEE: SMITHKLINE BEECHAM BIOLOGICALS 2002
PATENT NUMBER: WO 200232450 PATENT DATE: 20020425 WPI ACCESSION NO.: 2002-471376 (200250)
PRIORITY APPLIC. NO.: US 690921 APPLIC. DATE: 20001018
NATIONAL APPLIC. NO.: WO 2001EP11984 APPLIC. DATE: 20011016
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - New Immunogenic composition (I) comprises: (a) a cancer *antigen* (CA) e.g. MAGE or prostase *antigens* linked to heterologous fusion partner, prostase fragments comprising at least 20 amino acids of prostase, mutated prostase, P501S, Cripto, or Her2-neu derivatives devoid of...

... manufacture of a medicament for the treatment or prophylaxis of tumors. WIDER DISCLOSURE - The following are disclosed: (1) novel adjuvant formulations for use with cancer *antigens* , comprising saponin, immunostimulatory oligonucleotide, and optionally lipopolysaccharide. The adjuvant combinations may be used as both systemic or mucosal adjuvant, and represent a class of mucosal...

... that are suitable for application in humans to replace systemic vaccination by mucosal vaccination, and are used in the formulation of vaccines which may be *administered* via the systemic or mucosal route. The adjuvant combinations are suitable both for immunoprophylaxis of diseases and immunotherapy of diseases such as cancer; (2) a delivery device for systemic *administration* pre-filled with the vaccine or adjuvant compositions; (3) manufacturing vaccine or adjuvant by providing saponin, *CpG* molecule and admixing them with an *antigen*; (4) a mucosal vaccine composition comprising an *antigen* and a hemolytic saponin, and use of mucosal vaccine composition for treating an individual susceptible to or suffering from disease; and (5) use of the mucosal vaccine composition for inducing a systemic *antigen* -specific immune response in a mammal. BIOTECHNOLOGY - Preferred Composition: The composition further comprises a lipopolysaccharide such as monophosphoryl lipid A, 3-O-deacylated monophosphoryl lipid A, or diphosphoryl lipid A. The immunostimulatory oligonucleotide contains at least 2 *CpG* motifs and is any one of TCCATGACGTTCCTGACGTT (*CpG* 1826), TCTCCCAGCGTGCGCCAT (CpG1758), ACCGATGACGTCGCCGGTGACGGCACCACG, TCGTCGTTTTGTCGTTTTGTCGTT (*CpG* 2006), TCCATGACGTTCCTGATGCT (*CpG* 1668). The composition preferably comprises a saponin such as QS21. The saponin is formulated to form ISCOMS or liposomes. The saponin is present in an...

...additionally comprises the phosphorylation domain of Her 2 neu. ACTIVITY - Cytostatic; antimicrobial; antiallergic; immunosuppressive. MECHANISM OF ACTION - Vaccine. A range of adjuvant formulations with the *antigen* which was a fusion of the extracellular domain of Her 2 neu linked to the phosphorylation domain (ECD-PD) (ECD-PD with no adjuvant (group...

... liposomes with QS21 and with any of the adjuvant combinations 3D-MPL in membrane, tocol containing oil in water emulsion with QS21 and 3D-MPL *CpG*, liposomes with QS21 and 3D-MPL in membrane +*CpG*, tocol containing oil in water emulsion with QS21 and 3D-MPL+*CpG*, 3D-MPL+ *CpG*, QS21+*CpG*, tocol containing oil in water emulsion+*CpG*, liposomes with QS21 in membrane+*CpG* , liposomes with 3D-MPL in membrane+*CpG* (groups 2-11, respectively)) which was produced in Chinese hamster ovary (CHO) cells according to the methods of WO 00/44899, was investigated. Groups of B6F1 mice were vaccinated on four occasions (in 50 microlitres volumes), intramuscularly, 14 *days* apart. 14 *days* post the 4th vaccine dose, the mice were challenged subcutaneously with 2 x 10 (to the power of 6) TC1 tumor cell expressing the Her...

... tumor regression. USE - (I) is useful for treating a patient suffering from susceptible to a cancer expressing a Her 2 neu or prostate specific/tumor *antigen* . (I) is also useful for treating a patient suffering from or susceptible to a cancer expressing any of MAGE, prostase, P501S or Cripto (claimed). The formulations containing tumor *antigens* are useful for immunotherapeutic treatment of prostate, breast, colorectal, lung, pancreatic, renal, or melanoma cancers. (I) is useful for inducing an immune response in an...

... for treating a mammal susceptible to or suffering from an infectious disease or cancer, or allergy or autoimmune disease. (I) is useful as a medicament. *ADMINISTRATION* - The immunogenic compositions are *administered* by systemic or mucosal route. The vaccine compositions are thus *administered* by intramuscular, intraperitoneal, intradermal, transdermal, intravenous or subcutaneous route (systemic routes), or by intravaginal or intrarectal or intranasal route (mucosal route). No specific clinical dosages are given. ADVANTAGE - The immunostimulatory oligonucleotides (*CpG*) and saponin and optionally a lipopolysaccharide combination are extremely potent adjuvants. The oligonucleotides in the adjuvant and vaccine compositions act synergistically with the combined saponin/lipopolysaccharide in the induction of *antigen* specific immune responses leading to enhanced tumor regression. The formulations are potent in the induction of immune responses conventionally associated with Th-1 type immune system. Her 2 neu *antigens* that are formulated with 3D-MPL, QS21 and *CpG* oligonucleotide together with liposome or oil-in-water emulsion carrier, produce both a humoral and cell mediated response in comparison to the formulations containing only *CpG* that do not produce a significant cell-mediated immune response.(49 pages)

4/3,K/31 (Item 16 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0289309 DBR Accession No.: 2002-11156 PATENT
Fusion protein useful in vaccine compositions for treating allergies and asthma, comprises a Pathogen Associated Molecular Pattern and an antigen - recombinant fusion protein production for use in recombinant vaccine against cancer, asthma, allergy, herpes, infection, tuberculosis, etc.
AUTHOR: MEDZHITOV R M P D
PATENT ASSIGNEE: UNIV YALE 2002
PATENT NUMBER: WO 200209748 PATENT DATE: 20020207 WPI ACCESSION NO.: 2002-217100 (200227)
PRIORITY APPLIC. NO.: US 282604 APPLIC. DATE: 20010409
NATIONAL APPLIC. NO.: WO 2001US24228 APPLIC. DATE: 20010731
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - A fusion protein (I) comprising an isolated Pathogen Associated Molecular Pattern (PAMP), its immunostimulatory portion or derivative, and an *antigen* (II), its

immunogenic portion or derivative, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a recombinant vector (III) comprising nucleotides encoding (I); (2) a host cell (IV) comprising (III); (3) producing (I); (4) a vaccine (V) comprising (I); (5) treating (M1) a subject, by: (a) *administering* (V) and antibodies (Abs) or activated immune cells directed against (II), to a subject; or (b) *administering* (V) and a chemotherapeutic or anti-angiogenic agent; (6) stimulating (M2) an innate immune response in an animal and thus enhancing the adaptive immune response to a foreign or self-*antigen*; and (7) a vaccine comprising a PAMP conjugated with a foreign or self-*antigen* that stimulates an innate immune response in an animal and thus enhances the adaptive immune response to a foreign or self-*antigen* but does not lead to undesirable levels of inflammation. WIDER DISCLOSURE - The following are disclosed: (1) nucleic acid molecules encoding (I); (2) peptide mimetics of non-protein PAMPs; (3) derivatives, portions or peptides of PAMPs that are recognized by the innate immune system; (4) a chimeric construct comprising *CpG* or *CpG*-DNA, and an *antigen*; (5) a mimetic of a three-dimensional structure of PAMP protein or its *antigen* ; (6) conservative variants of naturally occurring protein PAMPs, peptides or peptide mimetics of PAMPs that recognize the corresponding PAMP receptor proteins; and (7) a combination...

... PAMP is bacterial lipoprotein (BLP) comprising a sequence of 78 amino acids fully defined in the specification. (II) is selected from any one of the *antigens* given in the specification. PAMP is a peptide mimetic of a non-protein PAMP and/or (II) is a peptide mimetic of a non-protein *antigen*. (I) comprises a leader sequence, glycosylation or lipidation consensus sequence and an *antigen* sequence. The leader sequence signals post-translational glycosylation or lipidation of the consensus sequence. The leader peptide comprises one of sequences of (A) - (E). The...

... M2, the innate immune response is stimulated by activating one or more Toll-like Receptors. The adaptive immune response is enhanced by the activation of *antigen* presenting cells (APCs) by the activation of one or more Toll-like Receptors. Met Lys Ala Thr Lys Leu Val Leu Gly Ala Val Ile...

... bone marrow-derived DC to produce interleukin (IL)-6 after stimulation in vitro was determined. Bone marrow dendritic cells were isolated and grown for 5 *days* in culture in the presence of 1 % granulocyte macrophage-colony stimulating factor (GM-CSF). After 5 *days*, cells were replated at 250000 cells/well in a 96-well dish and treated with either Ealpha peptide (0.3 micrograms/ml), lipopolysaccharide (LPS) (100...

... neurological diseases, cardiovascular diseases, immune deficiency syndrome, topical and systemic infections, leprosy, tuberculosis, shingles, warts, herpes, malaria, gingivitis, atherosclerosis and diseases associated with allergic reactions. *ADMINISTRATION* - A vaccine (V) comprising (I) is *administered* through parenteral, intravenous, oral, suppository or mucosal route (claimed). (V) is also *administered* through intramuscular, sub-cutaneous or intraperitoneal route. No dosage is specified. ADVANTAGE - The vaccine provides an efficient way of making and using a single molecule...

... immune response that activates other aspects of adaptive immune response. The vaccine provides an efficient way to produce an immune response to one or more *antigens* without adverse side effects normally associated with conventional vaccines. The vaccine induced an immune ... different fusion partners, the recombinant product may be localized to different compartments, or it might be secreted. The vaccine induces strong immune response against target *antigen* with minimal undesired inflammatory reaction, as well as minimal instances of autoimmune disease. EXAMPLE - In order to produce a model vaccine cassette, a Pathogen-Associated Molecular Pattern (PAMP) was fused to

the characterized mouse *antigen* , Ealpha. PMAP, a bacterial lipoprotein (BLP), was known to stimulate innate immune responses through the receptor, Toll-like-receptor-2 (TLR-2). The protein sequence (S1) of BLP used in the vaccine cassette for fusion with an *antigen* of interest comprised 78 amino acids, given in the specification. The leader sequence included amino acids 1 - 20 of S1. The first cysteine (amino acid...

... the yield of a recombinant vaccine, as the lysine can form a covalent bond with the peptidoglycan. To assist in identification and purification of the *antigen*, a hexa-histidine tag was engineered on the C-terminal of the protein. The final construct is given in the specification. The fusion protein was...

4/3,K/32 (Item 17 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0287201 DBR Accession No.: 2002-09048 PATENT
Treating or preventing cancer, such as basal cell carcinoma, comprises administering immunostimulatory nucleic acids that induce expression of cell surface antigens and antibodies to a subject having or at risk of developing cancer - CpG oligonucleotide immunostimulant for use in tumor and leukemia immunotherapy and diagnosis
AUTHOR: WEINER G; HARTMANN G
PATENT ASSIGNEE: UNIV IOWA RES FOUND 2001
PATENT NUMBER: WO 200197843 PATENT DATE: 20011227 WPI ACCESSION NO.: 2002-154611 (200220)
PRIORITY APPLIC. NO.: US 213346 APPLIC. DATE: 20000622
NATIONAL APPLIC. NO.: WO 2001US20154 APPLIC. DATE: 20010622
LANGUAGE: English

ABSTRACT: DERWENT ABSTRACT: NOVELTY - Methods for treating or preventing cancer comprising *administering* to a subject having or at risk of developing cancer, immunostimulatory nucleic acids that induce expression of cell surface *antigens* and antibodies, are new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are provided for the following: (1) a method (M1) for treating or preventing cancer, comprising *administering* to a subject having or at risk of developing cancer, an effective amount of a nucleic acid that upregulates CD20 expression, and an anti-CD20...

... cell surface marker induced on the B cell is indicative of the type of lymphoma; (3) a method (M3) for treating or preventing cancer, comprising *administering* to a subject having or at risk of developing cancer, an effective amount of a nucleic acid to induce expression of a surface *antigen* on a cancer cell surface, and *administering* to the subject an antibody selected from an anti-CD22 antibody or an anti-CD19 antibody; (4) a method (M4) for treating lymphoma, comprising isolating a B cell from a subject having lymphoma, identifying a surface *antigen* which is not expressed or which is expressed on the surface of the B cell in an amount lower than that of a control B cell, *administering* to the subject an antibody specific for the identified surface *antigen* and an immunostimulatory nucleic acid in order to treat the cancer, wherein the immunostimulatory nucleic acid is *administered* in an effective amount to upregulate expression of the surface *antigen* on the cancer cell surface; (5) a method (M5) for treating a lymphoma resistant to antibody therapy, comprising *administering* to a subject having a lymphoma resistant to therapy with an antibody specific for a surface *antigen*, an antibody specific for the surface *antigen* to which the lymphoma is resistant and a nucleic acid in order to treat the lymphoma, wherein the nucleic acid is *administered* in an effective amount to upregulate expression of the surface *antigen* on the lymphoma cell surface; (6) a method (M6) for treating cancer in a human, comprising *administering* to a human an immunostimulatory nucleic acid and an antibody of IgG1 isotype,

which binds to a cell surface *antigen* of a cancer cell and wherein the nucleic acid and the antibody are *administered* in an effective amount for killing the cancer cell; and (7) a kit, comprising a package including at least two containers, the first container housing an immunostimulatory nucleic acid, the second container housing an antibody specific for a cell surface *antigen*, and instructions for screening a cell to determine whether the immunostimulatory nucleic acid upregulates expression of the cell surface *antigen*. ACTIVITY - Cytostatic. Mice were injected intraperitonealy (i.p.) with 5000 T3C cells on *day* 0. They were then given 100 micrograms anti-idiotype monoclonal antibody as either IgG1 (MS5A10) or IgG2a (MS11G6) on *days* 5, 7, and 10. In this model, the target *antigen* was the idiotype expressed by the lymphoma cells. Therefore, the anti-tumor antibodies were also 'anti-idiotype'. These antibodies (MS5A10 and MS11G6) were simultaneously both anti-tumor antibodies and anti-idiotype antibodies. Twenty micrograms of *CpG* nuclease resistant phosphorothiate-modified oligodeoxynucleotide (ODN) 1826 (5'-TCCATGACGTTCCTGACGTT-3') was given at the same time. Untreated controls had a median survival time (MST) of 17 *days* after inoculation with tumor. Mice treated with murine IgG1 antibody plus *CpG* ODN had survival that was similar to those treated with murine IgG1 antibody alone (MST 28 *days* and 27 *days*, respectively). In contrast, mice treated with murine IgG2a plus *CpG* ODN had survival that was significantly improved when compared to mice treated with murine IgG2a alone (MST 45 *days* and 37 *days*, respectively). MECHANISM OF ACTION - The immunostimulatory nucleic acid molecules induce the expression of cell surface *antigens* such as CD20 on the surface of the cancer cell. The induction of these *antigens* leads to enhanced antibody-dependent cellular cytotoxicity (ADCC). USE - The methods are useful for treating or preventing cancer such as basal cell carcinoma, bladder cancer...

... cavity cancer (e.g., lip, tongue, mouth, and pharynx), ovarian cancer, pancreatic cancer, prostate cancer, rhabdomyosarcoma, skin cancer, stomach cancer, testicular cancer, and uterine cancer. *ADMINISTRATION* - The nucleic acid and antibody may be *administered* together or separately (claimed) by any known method of *administration*, e.g. orally, intranasally, rectally, subcutaneously, etc. The dosage is 0.1 microgram to 10 mg, preferably 10 micrograms to 1 mg per *administration* which can be daily or weekly. Parenteral doses range from 10 micrograms to 5 mg, preferably 100 micrograms to 1 mg per *administration*. (220 pages)

4/3,K/33 (Item 18 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.
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0285276 DBR Accession No.: 2002-07123 PATENT

Producing immature, activated or mature dendritic cells in vitro, ex vivo or in vivo, especially useful for immunotherapy of, e.g., tumors, comprises contacting dendritic precursors cells with interleukin-15 - vector-mediated interleukin-15 and granulocyte-macrophage colony stimulating factor gene transfer and expression in host cell for recombinant protein production and disease therapy

AUTHOR: BANCHEREAU J F; MOHAMADZADEH M; PALUCKA A K

PATENT ASSIGNEE: BAYLOR RES INST 2001
PATENT NUMBER: WO 200185920 PATENT DATE: 20011115 WPI ACCESSION NO.: 2002-089793 (200212)
PRIORITY APPLIC. NO.: US 203571 APPLIC. DATE: 20000511
NATIONAL APPLIC. NO.: WO 2001US15300 APPLIC. DATE: 20010511
LANGUAGE: English

...ABSTRACT: dendritic cells to form mature dendritic cells; (c) producing immature or activated dendritic cells from dendritic cell precursors in a patient by concurrent or sequential *administration* of IL-15 and at least one growth factor to the patient; or (d) producing mature dendritic cells from dendritic cell precursors in a patient by

concurrent or sequential *administration* of IL-15 at least one growth factor to the patient and at least one maturation agent. INDEPENDENT CLAIMS are also included for the following: (1) modulating (M2) an immune response in a patient comprising *administering* immature or membrane vesicles, or by *administering* mature dendritic cells to the patient or by concurrent or sequential *administration* of IL-15 and at least one growth factor to the patient; (2) producing (M3) isolated membrane vesicles comprising: (a) contacting dendritic cell precursors with...

... or stimulating dendritic cell differentiation (M4) from its precursors comprising contacting the precursors with IL-15 and at least one growth factor; (4) producing (M5) *antigen*-specific cytotoxic T lymphocytes in vitro or ex vivo comprising: (a) providing *antigen*-sensitized dendritic cells prepared by contacting its precursors with IL-15 and at least one growth factor and subsequent sensitizing of the dendritic cells t the *antigen*; and (b) contacting the *antigen*-sensitized dendritic cells with a population of cells comprising T lymphocytes to form activated *antigen* -specific cytotoxic T lymphocytes; (5) compositions comprising immature, activated or mature dendritic cells, membrane vesicles, *antigen*-specific cytotoxic lymphocytes, *antigen* -specific CD+4 T lymphocytes or dendritic cell precursors, which are produced by the methods cited above; and (6) producing (M6) dendritic cell precursors comprising...

... vitro or ex vivo with IL-15 to form dendritic cell precursors. BIOTECHNOLOGY - Preferred Method: (M1) further comprises sensitizing the immature dendritic cells to an *antigen*, preferably either prior to, during or after maturation. The maturation agent is selected from lipopolysaccharide, CD40L and poly(I):(C). (M3) also further comprises sensitizing the immature dendritic cells to an *antigen* prior to or after membrane vesicle release. The stimulation factor is selected from a cytokine, irradiation and low pH. The maturation agent is selected from *CpG* oligonucleotide and type I interferon. (M2) further comprises concurrent or sequential *administration* of at least one maturation growth factor to the patient. Increasing an immune response in a patient comprises *administration* of the *antigen*-specific cytotoxic T lymphocytes to the patient. Modulating immune response in a patient may also include *administering* *antigen*-specific CD+4 T lymphocytes. Preferred Interleukin: The IL-15 is in a form consisting of isolated IL-15 a recombinant IL-15 polypeptide, a...

... growth factor. Preferably, the growth factor is granulocyte-macrophage colony stimulating factor. ACTIVITY - Cytostatic; immunomodulator; antiallergic; antiasthmatic; immunosuppressive. No supporting data given. MECHANISM OF ACTION - *Antigen*-specific cytotoxic T lymphocyte (CTL) response inducer. IL-15 DCs were pulsed with Flu-MP peptide and used to stimulate purified CD8+ T cells. After two seven-*day* culture cycles performed in the presence of IL-7 (both cycles) and IL-2 (second cycle), the elicited T cells were able to efficiently kill...

... cells from dendritic cell precursors in vitro, ex vivo or in vivo. The dendritic cells may be used to modulate an immune response and produce *antigen*-specific cytotoxic T lymphocytes (all claimed). Furthermore, the dendritic cells are useful for immunotherapy of various pathologies, e.g., tumors or immune disease (e.g., allergy, asthma or autoimmune diseases). *ADMINISTRATION* - *Administration* is intravenous, intraarterial, intramuscular, intradermal or local (e.g. intra-tumoral or at the vicinity of a tumor site). No dosage given. EXAMPLE - Monocytes were...

... negative depletion using magnetic beads (98%) and cultured with interleukin-15 (IL-15) in combination with granulocyte-macrophage colony stimulating factor (GM-CSF). After six *days* of culture with medium containing GM-CSF+IL-15, characteristic phase contrast morphology of IL-15 dendritic cells (DCs) indicated extensive cell aggregation. Representative phase...

4/3,K/34 (Item 19 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0283766 DBR Accession No.: 2002-05613 PATENT
New immunostimulatory compositions comprising RNA/DNA hybrid oligonucleotides, useful for enhancing an immune response or inducing cytokines, particularly for treating diseases, e.g. cancer, allergy or HIV infection - nucleic acid vaccine useful in cancer, autoimmune disease, bacterium, virus infection gene therapy
AUTHOR: MOND J J; FLORA M; KLINMAN D M
PATENT ASSIGNEE: BIOSYNEXUS INC 2001
PATENT NUMBER: WO 200193902 PATENT DATE: 20011213 WPI ACCESSION NO.: 2002-130570 (200217)
PRIORITY APPLIC. NO.: US 209797 APPLIC. DATE: 20000607
NATIONAL APPLIC. NO.: WO 2001US18276 APPLIC. DATE: 20010607
LANGUAGE: English

...ABSTRACT: oligonucleotide comprising both an RNA region and a DNA region, where at least one terminus of the oligonucleotide comprises RNA, and at least one target *antigen*; (3) a method of stimulating innate immunity comprising *administering* at least one oligonucleotide comprising both an RNA region and a DNA region, where at least one terminus of the oligonucleotide comprises RNA, and where the oligonucleotide is associated with a physiological carrier or delivery system; (4) a method of stimulating global immunity comprising *administering* at least one oligonucleotide comprising both an RNA region and a DNA region, where at least one terminus of the oligonucleotide comprises RNA, and where the oligonucleotide is associated with a physiological carrier or delivery system; (5) methods of stimulating a cellular immune response or a humoral immune response comprising *administering* the vaccine of (Ib); and (6) a method of making a vaccine comprising associating: (a) at least one oligonucleotide comprising both an RNA region and...

... terminus of the oligonucleotide comprises RNA; and (b) a physiological carrier or delivery system. BIOTECHNOLOGY - Preferred Composition: The DNA region comprises at least one unmethylated *CpG* dinucleotide, where the DNA region comprises at least one *CpG* sequence. Preferably, both terminal comprise at least 1 RNA nucleotide. At least one terminus comprises poly A RNA. A linkage between at least two nucleotides...

... methods. Oligonucleotides DDD and RDR were added to the media of cultured cells to final concentrations of 0.3, 3, or 30 microg/ml. 24 *hours* after oligonucleotide addition, Th1 and Th2-type cytokine levels in the media were determined by enzyme linked immunoabsorbant assay (ELISA). The hybrid DNA/RNA oligonucleotides...
... composition is also useful for treating, preventing or ameliorating the symptoms resulting from exposure to a bio-warfare agent, e.g. Ebola, Anthrax or Listeria. *ADMINISTRATION* - *Administration* may be intravenous by bolus injection or continuous infusion, transcutaneous, intranasal, oral, gastric, intravaginal, intrarectal, oral, intramuscular or subcutaneous. In mouse, dosage is 001-1000...

4/3,K/35 (Item 20 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0261627 DBR Accession No.: 2001-01035
CpG DNA is an effective oral adjuvant to protein antigens in mice - oligonucleotide containing immunostimulatory CpG motif useful as vaccine adjuvant
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JOURNAL: Vaccine (19, 7-8, 950-57) 2000
ISSN: 0264-410X CODEN: VACCDE
LANGUAGE: English

ABSTRACT: *CpG* DNA, an effective oral adjuvant to protein *antigens* in mice, was studied. Groups of female BALB/c mice 8-10 weeks were immunized at *day* 0, 7 and 14 *day* by oral *administration* of 100-ug hepatitis B virus surface *antigen* (HBsAg) or tetanus toxoid (TT), alone or combined with 50, 100, or 500 ug of oligonucleotide containing immunostimulatory (*CpG*) made with a nuclease-resistant phosphorothioate. Control group mice were immunized with 100-ug TT with the non-*CpG* control oligonucleotide. All samples were collected over a 2 *day* period 1 week after third and final immunization. The results showed that oral delivery of HBsAg without adjuvant resulted in none or only anti-HBs immunoglobulin (Ig) G titers in the plasma of mice. In contrast, much high levels of anti-HBs IgG antibodies were detected when *CpG* was added, with highest titers and lowest variability being obtained with the 100-ug dose. When TT was used as *antigen*, TT-specifc IgG titers in plasma were from 15-20-fold higher than for any of three doses of *CpG* ODN than for TT alone. Results from this study indicate that stimulatory *CpG* ODN may be effective as adjuvant with oral vaccines. (30 ref)

4/3,K/36 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
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02040294 SUPPLIER NUMBER: 80632550 (USE FORMAT 7 OR 9 FOR FULL TEXT)
CpG Oligonucleotides Generate Antitumor Response In Rodents.
Gene Therapy Weekly, 3
Dec 13,
2001
PUBLICATION FORMAT: Newsletter ISSN: 1078-2842 LANGUAGE: English
RECORD TYPE: Fulltext TARGET AUDIENCE: Academic
WORD COUNT: 478 LINE COUNT: 00042

... rodents, including normal and macrophage depleted Fisher rats, and nude and SCID mice to perform their analyses of CpG-ODNs and immune system response.

Intermittent *administration* of *CpG*-ODNs to rats with normal macrophage levels up to 19 *days* after they were given subcutaneous inoculations of 9 L glioma cells resulted in significant reductions in tumor volume. In contrast, tumors continued to grow in control rats treated with normal saline. The effect of *CpG*-ODN therapy on tumor inhibition was seen in over a third of the treated rats, Auf and coworkers reported (Implication of macrophages in tumor rejection induced by *CpG* -oligodeoxynucleotides without *antigen*, Clinical Cancer Research, November 2001;7(11):3540-3543).

Tumor-specific long-term protective immunity was also evident, as cured rats rechallenged with injections of...
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